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PREMEDICATION WITH THE BARBITURATES.¹

By GILBERT BROWN, M.B., Ch.B. (Liverpool),
Adelaide.

SINCE the introduction of general anæsthesia the patient has been spared the physical agony of a surgical operation, but far too little attention has been given to the mental distress preceding and following this ordeal. Morphine injected in the usual dosage is quite inadequate to prevent the emotional disturbance attendant on being taken to the theatre, watching the preparations, and inhaling the fumes of an anæsthetic until unconsciousness supervenes. Nor does it eliminate the horror of the sleepless hours after awakening, distressed by the smell of ether, nausea, vomiting and pain. By the administration of the barbiturates it is possible to render the patient unconscious in his bed before

the anæsthetic is induced; or, at least, to produce a state of euphoria in which the further proceedings may be faced with the utmost calm. A further result is that the amount and concentration of the general anæsthetic are reduced, the period of unconsciousness is prolonged and followed by some hours of drowsiness, while vomiting is absent or slight and seldom remembered.

History.

The barbiturates first came into use in 1903, when Fischer and Mehring⁽¹⁾ introduced veronal. Since then a number of new compounds of barbituric acid have been produced and have been used as basal narcotics and even as anæsthetics in themselves. These include "Somnifaine", "Luminal", "Pernocton", "Dial", "Neonal", "Allonal", "Amytal", "Sodium amytal" and "Nembutal". These may be considered in detail.

Veronal.—Veronal (diethyl-barbituric acid) was found to be an excellent hypnotic and seda-

¹ Read at a meeting of the South Australian Branch of the British Medical Association on August 25, 1932.

tive,⁽²⁾⁽³⁾⁽⁴⁾ and before long it was used in conjunction with anaesthetics by a number of observers. Stossmann⁽⁵⁾ gave 1.0 gramme (fifteen grains) before chloroform anaesthesia. Stocker⁽⁶⁾ advised 0.45 gramme (seven and a half grains) to be taken on the night prior to operation, and considered it part of the anaesthesia. Strauch⁽⁷⁾ used it by the same method, but in a dose of 1.0 gramme (fifteen grains), while 0.518 gramme (eight grains) has been the favourite prescription of Professor Alexis Thomson⁽⁸⁾ for a number of years.

"*Somnifaine*."—"Somnifaine" (a solution of the diethylamine salts of diethyl and allyl iso-propyl barbituric acids) was used extensively in France⁽⁹⁾ and Germany,⁽¹⁰⁾ and to a less extent in America,⁽¹¹⁾ England⁽¹²⁾ and Australia.⁽¹³⁾ However, it has fallen into disfavour and has been discarded by many observers.⁽¹⁴⁾

"*Luminal*."—"Luminal" (phenyl-ethyl barbituric acid) is warmly advocated by Willard Bartlett,⁽¹⁵⁾ who gives a routine dose of 1.0 gramme (fifteen grains) by mouth, and follows it with nitrous oxide and oxygen. He states: "We have never known such freedom from respiratory complications." It has been avoided by many on account of its depressing effect on the blood pressure, which is said to be greater than that of veronal.⁽¹⁶⁾

"*Allonal*."—"Allonal" (allyl-isopropyl barbituric acid with phenyldimethyl-dimethylamine-pyrazolon), followed by nitrous oxide and oxygen, is recommended by Bellamy Gardner⁽¹⁷⁾ as an anaesthetic for dental extractions.

"*Amytal*."—"Amytal" (iso-amyl-ethyl barbiturate) was synthesized in 1923 by Shonle and Moment.⁽¹⁸⁾ It was used extensively on laboratory animals⁽¹⁹⁾⁽²⁰⁾⁽²¹⁾ and was then used in man for hypnotic and sedative purposes.

"*Sodium Amytal*."—"Sodium amytal" (sodium iso-amyl-ethyl barbiturate) was used for the induction of anaesthesia in laboratory animals and later was administered to human beings by intravenous injection. Zervas and McCallum⁽²²⁾ stated that:

Sodium iso-amyl-ethyl barbiturate, prepared in a ten per cent. solution for intravenous injection, is capable of controlling essentially any type of convulsions and of alleviating pain in certain conditions not responding to the routine therapeutic procedures. It has been used also in combination with other general or local anaesthetics for the induction of anaesthesia . . . It eliminated most of the undesirable effects experienced with ether induced anaesthesia, and the postoperative nausea, retching and vomiting. It is a safeguard to the life of the patient when given prior to the use of procain and cocaine.

At first it was used as the sole anaesthetic, but this was found to be objectionable, and later, smaller doses were used and supplemented by small amounts of inhalation anaesthetic. Lundy⁽²³⁾ reported its use in more than one thousand cases at the Mayo Clinic about the same time. He pointed out complications which might occur, such as marked fall of blood pressure when the injection was made too rapidly; oedema of the lungs and pneumonia when the dose was very large; the necessity for catheterization after 25% of abdominal operations; and the

post-operative danger of respiratory obstruction from the tongue falling back.

"*Nembutal*."—"Nembutal" or pento-barbital sodium [sodium ethyl-(1-methyl-butyl) barbiturate] was introduced in 1930 and tried extensively by Lundy,⁽²⁴⁾ who concluded that:

Intravenous anaesthesia by means of the barbiturates alone is not justified, because of occasional untoward result incident on their use. The drugs should be given in small rather than large doses.

Fitch, Waters and Tatum⁽²⁵⁾ confirmed this and reported:

We believe that the use of the quickly detoxified barbiturates may constitute in the future a very valuable background upon which to superimpose block or general anaesthesia. A nervous individual can be taken to the operating room asleep.

In 1931 Lundy⁽²⁶⁾ reported an experience of "Nembutal" in more than 2,300 cases. "Nembutal" was first used in England by Magill,⁽²⁷⁾ who states:

1. Intravenous injection of Nembutal provides a pleasant method of bridging the gap between consciousness and unconsciousness before general anaesthesia. 2. The amount of anaesthetic subsequently required is diminished. 3. Post-operative nausea and vomiting are diminished or absent. 4. The chief disadvantage is post-operative restlessness in a small percentage of cases (about 10 per cent.).

The intravenous method of administration was found to be unsuitable for some patients, so both "Sodium amytal" and "Nembutal" were used by the mouth in the form of capsules and were found to be quite satisfactory.

"*Pernocton*."—"Pernocton" (the sodium salt of the secondary butyl- β -bromallyl barbituric acid) was introduced in Germany, and by August, 1930, it had been used in more than 2,000 cases in Europe. It has also been used fairly extensively in America, where, in 1930, Friedlaender⁽²⁸⁾ gives a bibliography of 194. It has also been used to a less extent in England and in Australia.⁽²⁹⁾⁽³⁰⁾

Other barbiturates have also been used for pre-medication, but to a less extent; among them are "Dial"⁽³¹⁾ (diallyl barbiturate), "Neonal" (n-butyl-ethyl-barbiturate), and "Phanadorm"⁽³²⁾ (cyclohexenyl-ethyl barbiturate).

Pharmacology of "Sodium Amytal".

The pharmacology of "Sodium amytal" has been chosen as a type to illustrate that of all the derivatives of barbituric acid, for it has been shown by Zervas⁽³³⁾ that they have certain characteristics in common.

They are all primarily hypnotics; only occasionally will amounts ordinarily producing hypnosis produce analgesia or anaesthesia. Sufficiently large amounts will induce analgesia and anaesthesia in both animals and man. However, the dosage of such amounts precludes their routine use in man. The amount required to produce a given therapeutic effect bears approximately the same relationship to the fatal dose in each of these various compounds in their clinical application. All members of the barbituric acid series may depress the respiratory and circulatory systems when amounts large enough to produce deep hypnosis are administered.

Where there is any marked variation from the effects of "Sodium amytal" it will be indicated.

Metabolism.

Much controversy has arisen as to whether the blood sugar level is increased under "Sodium amytal" anaesthesia, and the opinions are about equally divided. Bolliger and Maddox⁽³⁴⁾ found that:

The usual immediate rise is evident at once after injection, but it is distinctly lower than with inhalation anaesthetics.

Bourne, Bruger and Dreyer⁽³⁵⁾ have shown that the injection of "Sodium amytal" is followed by a temporary kidney depression, but that the amount is less than that following the use of either ether or "Avertin". Emge and Hoffman⁽³⁶⁾ reported that patients who have received "Sodium amytal" and morphine as a preliminary to inhalation anaesthesia take more fluid in the twenty-four hours following the operation than patients receiving scopolamine and morphine. At the same time the urinary output is actually and relatively decreased in the "Sodium amytal" group. The intake was increased chiefly on account of the greater freedom from vomiting. Bolliger and Maddox showed that less "Sodium amytal" was required for those dogs whose blood urea was exceedingly high. Their experiments indicate that "Sodium amytal" is not very toxic to the kidneys, even in the presence of uraemia.

The liver function shows a slight transient depression, but no delayed damage; the harm would seem negligible.⁽³⁵⁾

The basal metabolism is slightly lowered by "Sodium amytal", but remains at a constant level, despite a fall of body temperature of two or three degrees. It is doubtful if the basal metabolic rate is decreased much below that of normal sleep.⁽³⁷⁾

Circulatory System.

The effects of "Sodium amytal" on the circulatory system are somewhat dependent on the amount, rate and manner of administration. In man, at the rate of one cubic centimetre of the 10% solution per minute, there is a decrease in both the systolic and diastolic blood pressures, and this effect is most marked if the injection is continued after the patient loses consciousness. As a rule, the blood pressures rise again within ten or fifteen minutes. Patients with hypertension and those debilitated may show a much greater fall in blood pressure.⁽³⁸⁾ The depression is increased by more rapid injection and is lessened when given by the mouth. The pulse rate may be increased slightly, but the effect is variable.

Respiratory System.

The respiration is usually regular in rate, but reduced in depth.⁽³⁹⁾ If "Sodium amytal" is accompanied by morphine, the effect is more intense. Animals given fatal doses of "Sodium amytal" died of respiratory failure, which usually precedes that of the circulatory system.

Central Nervous System.

"Sodium amytal" is more effective than opium derivatives in preventing fear.⁽⁴⁰⁾ When the drug

is injected intravenously, the induction is rapid and quiet. Mason, Baker and Pilcher⁽³⁸⁾ observed that, as the dose was increased, the patient became reflexly hypersensitive, and finally entered a profound state of narcosis. The pupils became contracted, and in some cases fixed, so that they would not react to light. The corneal reflex was diminished and the gag reflex remained intact. The knee jerks were often exaggerated during the period of hyperaesthesia. In this state patients sometimes became restless, if stimulated, and some time was required before they again became quiet.

The period of unconsciousness depends on the amount of the drug given, and may vary from three to ten hours. When a sufficient amount of the drug is eliminated, there may be a mildly restless period marked by disorientation, aimless movements and incoherent speech. When consciousness is regained, there is a period of amnesia during which the patient will answer questions, take drinks or food, but will be unable to recollect these incidents when questioned later. For a variable time afterwards they remain drowsy and sleep at intervals.

Further pharmacological details may be obtained from the articles of Zervas⁽³³⁾ and of Bolliger and Maddox,⁽³⁴⁾ both of which have been used extensively in compiling these notes.

Personal Experiences with the Barbiturates.

In 1909-1910, while acting as House Surgeon to the Hospital for Women, Shaw Street, Liverpool, I made a clinical research on the effects of narcotics combined with general anaesthesia.⁽⁴¹⁾ Among the drugs that were used was veronal in doses of 1.0 to 2.0 grammes (fifteen to thirty grains). The results were very satisfactory, although in one case there was an unduly prolonged period of sleep, as is shown by the following history.

CASE I.—Record 280 of March 11, 1910: Mrs. E.P., aged twenty-nine years, was given veronal, 2.0 grammes (thirty grains), one and a half hours before the time of operation. She was sound asleep when taken to the anaesthetic room and did not wake when the anaesthetic was begun, although there was slight struggling. C_2E_2 (a mixture of two parts of chloroform and three parts of ether) was dropped on the mask and 8.0 cubic centimetres (two fluid drachms) were required for the induction, which was complete in four minutes. Professor Briggs then performed a perineorrhaphy in twenty-six minutes, and the total amount of anaesthetic used was 20.0 cubic centimetres (five fluid drachms). The anaesthesia was very quiet and regular. It was noticed that the pupils were small throughout. The patient slept for twelve hours, and after a drink slept for another twelve hours. In all, she slept for about fifty hours, waking only four times for drinks. It was possible to rouse her and to obtain an answer to questions, but immediately afterwards she went to sleep again. She had no recollection concerning the operation and was most enthusiastic when comparing her comfort with that of several previous operations performed under ether anaesthesia without any premedication.

However, I abandoned the use of veronal after using it seven times, on account of the number of reports of poisoning and suicide by means of veronal that appeared in the medical Press about that time. Since then I have used it, or its British Pharma-

copœia equivalent, barbitone, occasionally as a pre-narcotic, instead of morphine, in patients whose renal efficiency was poor.⁽⁴²⁾

CASE II.—Record 287 of May 13, 1930: Mrs. C.W., aged seventy years, was a very frail old woman suffering from a large calculus hydronephrosis on the left side, and she also had a calculus in the right kidney. Her renal efficiency was very low, and it was considered unwise to give her any morphine. Barbitone, 0.6 gramme (ten grains), was given by the mouth one and a half hours before operation. Ethylene and oxygen were administered by the endotracheal method, while Sir Henry Newland drained the tumour and removed the calculus on that side. The operation required twenty-nine minutes and the recovery was good.

During the last four or five years I have prescribed barbitone in doses of 0.45 to 0.6 gramme (seven and a half to ten grains) to private patients on the night prior to operation. If possible, all preparations are completed before this dose is given and the patient is allowed to sleep undisturbed until next morning. I have never been able to see that anything beneficial can accrue from waking the patient at intervals throughout the night to give aperients or enemata and to wash and paint the skin. In fact, the routine administration of even an enema is unnecessary in the majority of operations, unless rectal injections are required after the operation. By being assured of a good sleep the patient is greatly benefited by lessening of apprehension and of psychic shock. This form of premedication is not shown on my records, and so it is not possible to give the exact number of patients to whom it was given, but the number must be between 700 and 800.

"Sodium Amytal."—Early in 1930 Messrs. Eli Lilly and Company were kind enough to send me supplies of "Sodium amytal" for intravenous injection; it was for clinical trial only and was not put on the market. It was supplied in ampoules containing 1.0 gramme (fifteen grains), in the form of a sterile powder, and was accompanied by other ampoules containing ten cubic centimetres of redistilled water. The makers also supplied literature and suggested a dosage of 20 to 25 milligrammes per kilogram of body weight, with a maximum dose of 1.6 grammes. They advised that a 10% solution should be used and injected not more rapidly than 1.0 cubic centimetre per minute.

I found that after a few cubic centimetres had been injected, the patient became sleepy, with a little more he went quietly to sleep, and with the full dose the sleep became so profound that it was possible to perform operations without any other anæsthetic.

CASE III.—Record 958 of July 4, 1930.—J.W., aged thirty-nine years, weight 53.5 kilograms (112 pounds), was suffering from a large rodent ulcer of the forehead, which infiltrated the frontal bone. He was given 1.0 gramme (fifteen grains) of "Sodium amytal" intravenously, and good anæsthesia resulted. Sir Henry Newland excised the ulcer widely and chiselled away the outer table of the frontal bone without any other anæsthesia being required. Movement of the arms took place when the supraorbital nerve was pulled upon. The patient slept for five hours and dozed until the following day, but could be roused to take drinks. He had no recollection of the operation.

Careful records were kept of all cases and a blood pressure chart was made in every instance. I soon felt, however, that the dosage was too large for safety, as there was not enough control once the injection had been made, and also that the period of post-operative unconsciousness was too great. The amount of the drug was consequently reduced and only just enough was given to render the patient unconscious. Local or inhalation anæsthesia was then added. With local anæsthesia the results were poor, as sometimes restlessness occurred and movements took place. With general anæsthesia the results were very satisfactory; both the amount and the concentration of the inhaled drugs were much lessened. Sometimes local and general anæsthesia were combined, as in Case IV (see accompanying anæsthesia record).

CASE IV.—Record 588 of September 4, 1930: S. Le B., an old man of eighty six years, was suffering from a carcinoma of the caecum. He had many other disabilities, which included cardiac insufficiency, which required digitalin, a chronic cough with some crepitations at the bases of the lungs, double inguinal hernia, and an enlarged prostate, which had been causing symptoms for eight years. While in bed he was given 0.7 gramme of "Sodium amytal" intravenously; he went to sleep and was transferred to the operating theatre, and the abdominal wall was infiltrated with "Novocain" solution. At this time his systolic blood pressure fell 28 millimetres of mercury, so 50 milligrammes of ephedrine were injected subcutaneously and the pressure rose to slightly above his normal reading. The operation was begun and continued until the peritoneum was opened, when he moved his arms and strained. A small amount of ether was given by the "open" method, while the caecum was resected and an ileo-colostomy performed by Dr. L. C. E. Lindon. The duration of the whole operation was two hours and five minutes and, though ether was given for an hour of this time, only 60 cubic centimetres (two fluid ounces) were required. The condition before and after operation was:

	Pulse.	Respiration.	Blood Pressures (millimetres of mercury).
Before ..	66	16	118-60
After ..	108	24	118-70

It was probably unwise to use "Sodium amytal" in a man whose lungs showed definite abnormalities, but no exacerbation of the chest symptoms occurred.

He slept for ten hours and then dozed until next morning, when he asked the nurse how much longer the preparations would take and when the operation was to be performed. He was delighted to hear that the operation was over, but complained that I had "stolen twenty-four hours".

Later, in 1930, the makers forwarded to me supplies of "Sodium amytal" in capsules of 0.2 gramme (three grains) for oral administration. One capsule is usually given on the night prior to operation and two are given two hours before operation. If a larger dose is required, it is better to give part of it three hours before operation. Morphine and atropine are given if required. A smaller dose is sufficient in patients over fifty-five years of age, frail or debilitated patients, and those with signs of renal deficiency or hypothyroidism. The oral method has proved satisfactory, although, of course, the amount of sedative effect cannot be gauged as accurately as when the drug is injected intravenously. Consequently some patients are not quite asleep, but their sensibilities are dulled and

ANAESTHESIA RECORD

MEMORIAL

Hospital ADELAIDE

City SOUTH AUSTRALIA

No. 987

WARD

DATE

4.9.30

NAME

S.A.I. LEB.

AGE

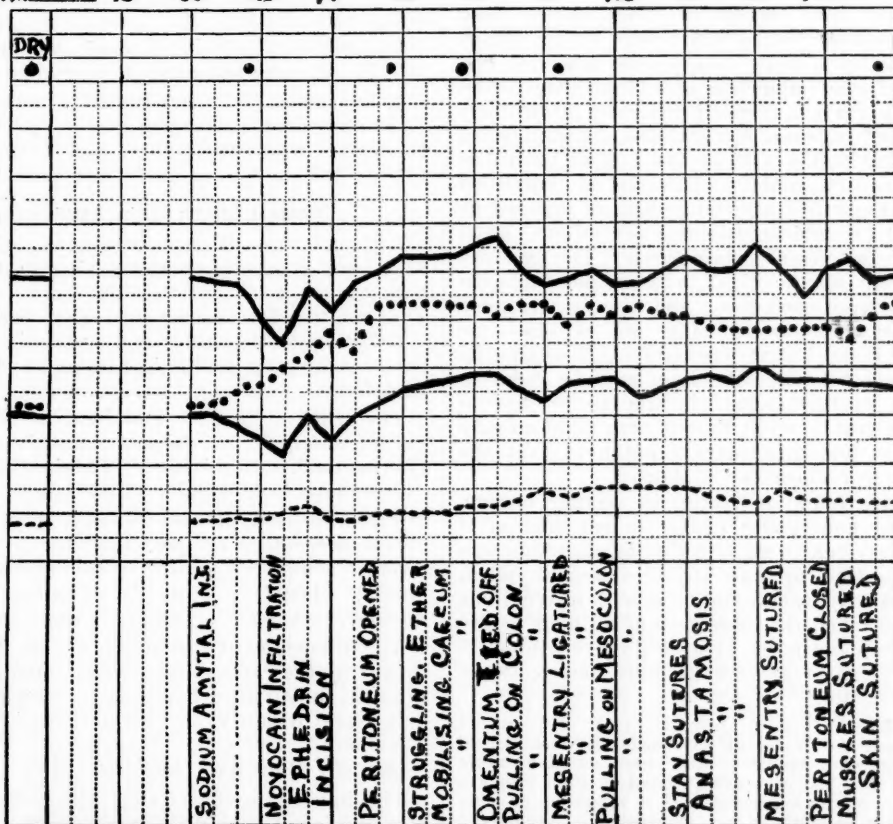
86

SURGICAL
RiskA
B
C ✓

OPERATION PROPOSED EXCISION OF CARCINOMA OF CAECUM

PHYSICAL FINDINGS NORMAL EXCEPT SURGICAL CONDITION, MYOCARDITIS,
CREPITATIONS AT BASES, ENLARGED PROSTATE, HERNIAE, OLD AGEPRELIMINARY HYPNOTIC MORPHINE AND ATROPINE DOSE $\frac{1}{64}$ $\frac{1}{100}$ TIME OF ADMIN. 9.15HOUR { A.M. 10
P.M. 15 30 45 11 15 30 45 12 15 30 45 1DOSAGE
SKIN
PUPIL180
160
140
120
100
80
60
40
20
0

REMARKS



SODIUM AMYTAL

CODE: • PULSE • RESP. ✓ B.P.

SEE

ANESTHETIC NOVOCAIN, ETHER TECHNIC. COMBINED

AMOUNT. RECORD 588

SURGEON L.C.E. LINDON

ANESTHETIST GILBERT BROWN

OPERATION ILEO-COLOSTOMY AND EXCISION OF CARCINOMA
OF CAECUM

REGAINED CONSCIOUSNESS AT 10.15 P.M. O'CLOCK

VOMITING

NONE
SLIGHT
EXCESSIVE

CIRC.

DEPRESSION

1ST ✓
2ND
3RD
SHOCK

CONVALESCENCE NORMAL EXCEPT FOR

they frequently have no recollection of being taken to the operating theatre, even when they have conversed with the surgeon and anaesthetist. All those who had been previously anaesthetized without "Sodium amytal" were most enthusiastic as to its benefits, and on subsequent occasions have demanded "some more of those green capsules". I found that "Sodium amytal" was a very useful premedication in combination with spinal or local anaesthesia, when it was limited to the amount required for a sedative effect only, as then the patient could still cooperate. If sufficient was administered to cause a hypnotic effect, there was frequently restlessness, which could be overcome only by adding some general anaesthetic. This has also been reported by Blakemore.⁽⁴³⁾

"Nembutal."—A supply of "Nembutal", also known as pentobarbital sodium, was kindly put at my disposal by Abbott Laboratories Limited, and was in two forms—ampoules of 0.45 gramme (seven and a half grains) in sterile powder for intravenous injection, and capsules for oral use, containing 0.1 gramme (one and a half grains). The former is dissolved in 10.0 cubic centimetres of redistilled water, making a 5% solution, which is injected at the rate of 1.0 cubic centimetre per minute, until the patient just loses consciousness. The capsules are given, one on the night prior to operation, in order to assure a good sleep, and also as a test for idiosyncrasy. In the morning two capsules are given one hour before operation. Morphine is usually given also, but the dose may be reduced. The action of "Nembutal" is similar to that of "Sodium amytal", except that it acts more quickly and is also eliminated more rapidly, so that the period of unconsciousness is shorter.

I have also found it useful, in smaller dosage, for patients undergoing dental extractions at a dental surgery, where an injection of morphine was impossible. One or two capsules are supplied, according to body weight and type, with instructions that they be taken three-quarters of an hour before the time of appointment. I have given "Nembutal" to a small number of children only, but one case is worth recording.

CASE V.—Record 546 of July 28, 1932: Dr. Rupert Magarey asked me to see an extremely nervous girl of eight years, who required an operation for acute appendicitis. She had been anaesthetized on eight previous occasions and it was suggested that it might be possible to do it this time without her knowledge. "Nembutal", 0.06 gramme (one grain), was given to her, dissolved in water. After twenty minutes she was just as awake as ever, and so another 0.1 gramme (one and a half grains) was given, and twenty minutes later she was fast asleep. Anaesthesia was induced without awakening her, and she was taken to the operating theatre. The appendix was removed and the child returned to bed after an anaesthesia of fifty-five minutes, during which 60.0 cubic centimetres (two fluid ounces) of ether were required. Consciousness returned two hours later, when morphine had to be given on account of restlessness.

"Pernocton."—A supply of "Pernocton" was kindly placed at my disposal by Messrs. Riedel de Haen, Incorporated. It is a 10% solution of the sodium salt of secondary butyl- β -bromallyl bar-

bituric acid, and is supplied in ampoules of 2.2 cubic centimetres. It was injected intravenously at the rate of 0.25 cubic centimetre per fifteen seconds. Consciousness was lost fairly quickly and without unpleasant symptoms. The amount of inhalation anaesthetic required was small.

"Allonal."—One tablet of "Allonal" has been given by mouth one hour before ethylene and oxygen anaesthesia. The sedative effect has been good, and this appears to be a useful form of premedication when an injection of morphine cannot be given. In one case in which it was used before an operation on the eye, a considerable amount of vomiting followed.

"Dial."—One tablet of "Dial" has been given by mouth one hour before ethylene and oxygen anaesthesia.

"Somnifaine."—I have used "Somnifaine" by mouth, but have not given it intravenously.

"Phanadorm."—I have used "Phanadorm" only on one occasion before gas and oxygen anaesthesia, the result was satisfactory, and I hope to make further trials.

General Effects of the Barbiturates.

Although the different compounds of barbituric acid have, generally speaking, similar effects, their true values as premedication vary considerably. The relationship found to exist between their toxicity, hypnotic values and premedication values has been investigated⁽⁴⁴⁾ in rats and is stated to be as follows.

The order of toxicity (minimal therapeutic margin of safety) from high to low is as follows: "Pernocton", "Barbitone", "Luminal", "Amytal", "Phanadorm", "Allonal", "Dial", and "Nembutal".

The order of hypnotic efficiency, as judged by the lowest percentage of the lethal dosage required to produce complete hypnosis is (high to low): "Nembutal", "Dial", "Allonal", "Phanadorm", "Pernocton", "Amytal", "Luminal", and barbitone.

The premedication efficiency (high to low), as judged by the ratio of effective to lethal dosage, the minimal duration of hypnosis to complete recovery and fewest disagreeable side actions, is as follows: "Nembutal", "Dial", "Allonal", "Phanadorm", "Amytal", "Luminal", barbitone, and "Pernocton".

The immediate effects vary also with the means of administration. With intravenous injection the hypnotic effect is achieved in a few minutes. When the drug is given by the mouth, the effect is delayed considerably. "Nembutal" causes sleep in from fifteen minutes to one hour; "Sodium amytal" is slower in action and its optimum effect is obtained in about two hours. With all the barbiturates the patient gradually becomes drowsy, the eyelids droop, speech is affected, words are slurred, yawning takes place, until gradually and quietly unconsciousness is attained.

The sequence was well demonstrated by a girl who was knitting when "Nembutal" was given by the mouth. After ten minutes she dropped a stitch, at the end of fifteen

minutes the mistakes in knitting were many, and five minutes later the knitting fell from her hands and she was asleep.

When the dose has been just sufficient to cause sleep, it is noticed that the pupils are small, and in some cases fixed, so that they do not react to light. The corneal reflex is diminished, but the cough reflex is retained and may be easily provoked by a strong vapour of ether. The pulse rate is little altered, though it may be increased; in very apprehensive patients it gradually decreases to normal as the sedative effect is produced. The blood pressures fall somewhat; when the drug is given by the mouth this depression is usually small, from 5 to 20 millimetres. When the drug is given by the intravenous method, the fall of blood pressure varies with the different drugs employed, the total amount given, and the rate of injection. In some of the earlier cases this fall was probably greater, as the solution was injected in doses of 1.0 cubic centimetre, with intervals of one minute, and so possibly some "speed shock"⁽⁴⁵⁾ may have been present. The effect on the systolic blood pressure noted in this series is shown in the accompanying table.

On one or two occasions, where the fall appeared to be excessive, a hypodermic injection of 50 milligrammes (three-quarters of a grain) of ephedrine was given and the blood pressure rose again. It is well to remember that ephedrine may raise the blood pressure while it is falling, but that it is not so effective when the fall is completed.

The respiration rate was not appreciably affected by the drugs, but the depth of respiration was often decreased.

Nausea appeared to be definitely decreased by all the drugs used, although this may in part be due to the partial amnesia of the post-operative period. Vomiting was certainly lessened in the patients who had intravenous injections, and appeared to be lessened in those who had the drugs by mouth. This is a point about which it is difficult to be certain, unless a very large number of cases are compared with an equally large number of controls. But there were only six of the 268 cases in which vomiting was excessive. A number of the patients had operations for tonsillectomy and drainage of the sinuses, and many of them vomited blood afterwards; but this is common in similar patients who have had no premedication by barbiturates. However, many of the patients had no recollection of vomiting and very few were depressed by it.

Sometimes there was excitement and restlessness before full consciousness returned. This was readily subdued by an injection of morphine. Apart from this, there was seldom any need for morphine on the first night.

Catheterization was required after some abdominal operations, but the frequency did not appear to be more than usual. In pelvic operations it is wise to ask the patient to pass urine before the drug is given, as otherwise they may go to sleep and have to be catheterized when on the operating table.

Special Indications for Use of the Barbiturates.

Barbiturates are indicated firstly for extremely nervous patients, especially those who have had many anaesthetics previously.

CASE VI.—Record 651 of September 26, 1930: R.Y., aged fourteen years, was an extremely nervous boy who had required six previous anaesthetics for plastic facial repairs after severe burns. When ether had been given he screamed, shouted, vomited, and it required four people to prevent him from getting off the table. He allowed an intravenous injection of "Sodium amytal", and was asleep after 0.8 gramme (twelve grains) had been given. Ethylene and oxygen were given by the endotracheal method while Sir Henry Newland replaced the tube pedicles.

Barbiturates are indicated secondly for powerful, alcoholic, muscular men, with whom struggling may be expected during the induction of anaesthesia.

CASE VII.—Record 784 of November 22, 1930: Mr. P., aged sixty-one years, was a bull-necked man, weighing 101.6 kilograms (223 pounds). He smoked half a pound of strong tobacco per week and drank about a bottle of whiskey per day. The intravenous injection of 0.8 gramme (twelve grains) of "Sodium amytal" sent him to sleep, and it was then an easy matter to give him ether and pass the endotracheal catheter, after which Dr. Matison performed an operation on his antrum. He slept for an hour and a half after operation and had no vomiting. When subsequently he required a further operation, he demanded that the anaesthetic should be given in the same manner.

Complication and Deaths.

It has been thought wise to include all the complications and deaths that occurred in this series of 268 cases, so that the record may be complete and impartial. The administration of the barbiturates certainly cannot be blamed for them all. Some of the complications are only trivial, and some occurred in patients who exhibited what are now known to be contraindications to the use of these drugs. Therefore, two groups have been made. In the first are included all cases in which it may be considered that the barbiturates may have been responsible to a greater or less degree; in the second are those cases with complications which have definitely no relation to the barbiturates administered.

Group I.

Group I comprises complications and deaths in which the barbiturates may have been in some measure responsible.

Drug.	Blood Pressure Raised.	No Fall.	Maximum Fall.	Minimum Fall.	Average Fall.
"Sodium amytal".	0	0	50-54%	7-10%	10-95%
"Pernocton"	0	1 case	23-43%	3-59%	11-83%
"Nembutal"	1 case (9-37%)	2 cases	41-17%	1-54%	9-87%

Respiratory Complications.—There have been respiratory complications in eight cases, of which three were slight and five were more serious; in the latter group three patients died. The slighter manifestation consisted of an exacerbation of a cold and two cases of mild bronchitis.

CASE VIII.—Exacerbation of a Cold—Record 831 of November 19, 1931: Miss M.G., aged forty years, weight 82.5 kilograms (182 pounds), was suffering from gall-stones, but her operation had been postponed for three days on account of a cold. "Sodium amytal", 0.4 gramme (six grains), was given by the mouth and was followed by ether given by the endotracheal method. Cholecystectomy and appendicectomy were performed by Sir Henry Newland. There was a slight exacerbation of the cold for two days.

CASE IX.—Bronchitis—Record 406 of June 3, 1931: R.D., aged forty-eight years, was given 0.45 gramme (seven and a half grains) of "Sodium amytal" intravenously, a dose which was not quite sufficient to send him to sleep. Ether was administered by the "open" method, while Sir Henry Newland performed an exploratory laparotomy. An anaesthesia of thirty-five minutes required 120 cubic centimetres of ether. The operation was followed by mild bronchitis for four days. His notes recorded that he had suffered from an attack of bronchitis four weeks previously.

CASE X.—Bronchitis—Record 89 of February 6, 1931: R.S., aged twenty-six years, was a half-caste aboriginal, weighing 96 kilograms (212 pounds). He received 1.0 gramme (fifteen grains) of "Sodium amytal" intravenously, followed by 120 cubic centimetres (four fluid ounces) of ether given by the "open" method during an operation for repair of a large inguinal hernia; the operation lasted one hour. Slight bronchitis occurred for three days after operation.

The more serious respiratory complications were: Hypostatic congestion of the lungs in two patients, one of whom died; apneumotosis and pulmonary oedema, each in one patient, both of whom died; and very slight pneumonia in a patient who recovered.

CASE XI.—Hypostatic Congestion of the Lungs, Recovery—Record 658 of September 30, 1930 (the same patient as in Case IV above): S. Le B., aged eighty-six years, had a faecal fistula following excision of a carcinoma of the caecum. He was subject to attacks of bronchitis, had a chronic cough and some crepitations at the bases of the lungs. He had some cardiac insufficiency, for which he was taking digitalin. "Sodium amytal" had been given to him intravenously on two previous occasions. Each time difficulty had been experienced in introducing the cannula into the vein, as the veins were small and thick walled. On this occasion it was found impossible to pierce a vein until one was dissected up. "Sodium amytal", 0.3 gramme (four and a half grains) was injected and the patient taken to the operating theatre, still talking. Ether was administered by the "open" method while Dr. L. C. E. Lindon performed a further ileo-colostomy and divided and closed the open ends of the ileum. The operation required one hour and ten minutes, during which time 100 cubic centimetres of ether were used. The patient stood the operation well and was conscious two hours later. Two days later there was hypostatic congestion of the lungs, and on the following day he was unconscious and cyanosed. He had passed hardly any urine during the previous twenty-four hours and appeared to be moribund. "Coramine" was injected intravenously into a small vein on the back of the hand, and his condition improved immediately. "Coramine" was given for a week by both the intravenous and oral routes. He recovered and lived for seven months, to die of shock after a long and difficult operation for prostatectomy, performed under ethylene and oxygen anaesthesia on May 20, 1931.

CASE XII.—Hypostatic Congestion of the Lungs, Death—Record 364 of May 25, 1932: Mr. F. S., aged sixty-six years,

weight 69.8 kilograms (156 pounds), was suffering from an impacted incisional hernia following an operation for perforated gastric ulcer. He also had crepitations at the bases of the lungs, but this fact was not reported to the anaesthetist. He received a hypodermic injection of morphine, 0.01 gramme (one-sixth of a grain), and atropine, 0.0006 gramme (one one-hundredth of a grain), and this was followed by an intravenous injection of 3.0 cubic centimetres of "Pernocton". He went to sleep and was taken to the operating theatre, where ether was administered by the endotracheal method, Mott's apparatus being used. Dr. Pomroy repaired the hernia by a modified Mayo's method, a procedure requiring one hour and sixteen minutes, as many adhesions had to be separated and some omentum excised. He was returned to bed in the second stage of circulatory depression. The figures were as follows:

	Pulse.	Respiration.	Blood Pressures (millimetres of mercury).
Before operation	84	20	122-80
After operation	120	24	90-60

Consciousness returned five and a half hours later, and a good night was passed. On the second day his temperature fell to 35° C. (95° F.), his pulse rate increased to 140 and he vomited. In spite of treatment with the shock cradle, intravenous injection of glucose-saline, and injections of pituitary extract and strychnine, he died at 5 p.m.

At the *post mortem* examination there were found to be hypostatic congestion of the lungs and slight interstitial nephritis.

CASE XIII.—Apneumotosis, Death—Record 471 of July 6, 1932: Mrs. L.B., aged fifty-four years, weight 87.1 kilograms (190 pounds), was given a hypodermic injection of morphine, 0.01 gramme (one-sixth of a grain), and atropine, 0.6 milligramme (one one-hundredth of a grain), followed three-quarters of an hour later by an intravenous injection of 3.5 cubic centimetres of "Pernocton", a very small dose for her weight. She fell asleep and was taken into the operating theatre, where ether anaesthesia was induced by the "open" method. Dr. Pomroy removed the gall-bladder and the appendix. The operation, which was difficult on account of the patient's obesity and the high position of the liver, required one hour and seventeen minutes, during which 160 cubic centimetres of ether were used. The pulse, respiration and blood pressure readings were as follows:

	Pulse.	Respiration.	Blood Pressures (millimetres of mercury).
Before operation	84	22	128-80
After operation	96	28	90-64

Consciousness was regained five hours later, and she spent a fair night after an injection of 0.015 gramme (one-quarter of a grain) of morphine, although the pulse rate rose to 128 and the respiration varied from 32 to 40. Next morning, at 9 o'clock, she complained of abdominal pain, and at 4 p.m. she vomited several times, her pulse rate was 144, the respiration was 52 per minute, and there was some abdominal distension. She was given an enema and an injection of pituitary extract, but her pulse became weaker and death took place at 12 midnight. A *post mortem* examination was performed and it was found that there was extensive collapse of the bases of both lungs—the bases were almost airless; there was considerable extravasation of bile between the liver and diaphragm, and the stomach was somewhat distended.

The condition of collapse of the lungs was not diagnosed before death, otherwise this patient might have been saved by the inhalation of carbon dioxide and oxygen. It is a wise precaution in at least all upper abdominal operations to administer inhalations of "10-90" (a mixture of 10% of carbon dioxide and oxygen 90%) for five minutes every three or four hours during the first twenty-four hours. By this means the lungs may be properly

expanded; it is painless or even pleasant to the patient, although he cannot take deep natural breaths owing to the pain of the wound.

It has been suggested⁽⁴⁶⁾ (47) that the prolonged period of post-operative quiescence caused by basal narcotics tends to produce pulmonary complications, and at first I was inclined to place the blame entirely on the "Pernocton"; but within a few weeks the same condition of apneumatosi was discovered at two other autopsies at the Adelaide Hospital.⁽⁴⁸⁾ In these two patients no basal narcotic had been given, the anæsthetic was ether, and the surgeons and anæsthetists were different. In all of these three cases there was a considerable amount of bile between the liver and the diaphragm.

The exact ætiology of apneumatosi is still uncertain, and Van Allen and Adams⁽⁴⁹⁾ state:

It is a curious circumstance that air which is imprisoned within the normal lung under conditions of quiet respiration remains without absorption for a long time, if, indeed, it is ever absorbed.

CASE XIV.—Acute Œdema of the Lungs, Death—Record 3 of January 5, 1931: Mrs. R., aged seventy-nine years, was sent to me by Dr. Shorney for examination as to her fitness for general anæsthesia for the cauterization of a rodent ulcer of the cornea. She was a very frail, thin woman, her weight being only 35.8 kilograms (seventy-nine pounds). She gave the history of coughing up blood ever since the age of fifteen, and said that this condition had been worse since the age of fifty-two, although no doctor had ever found any "lung disease". There were a few râles to be heard in the lungs, but no other abnormality could be detected. The heart sounds were faint, the pulse rate was 84 per minute, and the systolic and diastolic blood pressures were 170 and 110 millimetres of mercury respectively. The result of the breath-holding test was 35 seconds, which is within normal limits. Her urine contained neither albumin nor sugar. It was decided that she was fit for a short operation under nitrous oxide and oxygen anæsthesia.

Three hours before operation she was given 0.2 gramme (three grains) of "Sodium amytal" by mouth, but no morphine and atropine. Nitrous oxide and oxygen were administered by the endotracheal method for one hour and forty minutes while the following operation was performed. An external canthotomy was made, rodent ulcers on both eyes were treated with the electric cautery, that on the right eye was covered in by a flap of conjunctiva, and that on the left by a graft of mucous membrane from the lip. The anæsthetic was well borne throughout, and she was returned to bed in fair condition at 6.40 p.m. I did not see her afterwards, but have read the notes of her after-history, which show that at 8.30 p.m. some blood-stained mucus was coughed up, her pulse rate was 98. At 9.45 p.m. she was still coughing, and syrup of codein was given; her pulse rate was 100. At 11.30 p.m. the cough was very troublesome and the pulse rate was 120. At 2 a.m. her respiration increased for the first time from 24 to 40. Half an hour later the breathing was very distressed, and she was "coughing up a lot of frothy fluid". She was quite conscious and complaining of inability to breathe. In spite of oxygen, carbon dioxide, ephedrine and brandy, she gradually became worse and died at 3.20 a.m. The cause of death was presumed to be acute Œdema of the lungs.

It has been shown clinically that old people will stand an operation of forty minutes fairly well, but after that the risk is increased; operations lasting more than an hour have a much increased mortality. The only other case of acute post-operative pulmonary Œdema I have seen was one in which no barbiturate was given.

CASE XV.—Slight Pneumonia, Recovery—Record 546 of July 28, 1932 (see Case V); A.L., aged eight years, received 0.162 gramme (two and a half grains) of "Nembutal" by mouth before an operation for acute appendicitis. Four days later her temperature rose, and a small patch of pneumonia was discovered in one lung. The condition was not serious and the recovery was rapid.

It is interesting to notice that of these eight patients who had pulmonary complications, four showed some abnormality in the lungs before operation, and one of them had suffered from bronchitis four weeks previously. Latterly I have avoided the use of the barbiturates in any patient showing any signs of abnormality in the lungs. Since this paper was written I have seen a case of pneumonia following an operation on the antra in a patient suffering from marked bronchiectasis. It had been decided to give "Nembutal" to this patient, but, on finding out the lung condition, I prevented it from being given; otherwise the barbiturate might have been blamed.

Prolonged Unconsciousness.—Prolonged unconsciousness has been met in three patients, all of whom recovered. One has already been considered when I was referring to veronal (Case I).

CASE XVI.—Prolonged Unconsciousness—Record 561 of August 4, 1932: Miss R., aged forty-eight years, weight 79.3 kilograms (133 pounds), was given 0.2 gramme (three grains) of "Nembutal" by mouth and an injection of morphine, 0.008 gramme (one-eighth of a grain), and atropine, 0.00065 gramme (one-hundredth of a grain), followed by ether. Dr. L. G. Muirhead performed a subtotal hysterectomy, which required one hour and twenty minutes. The patient was unconscious for thirteen hours and very drowsy for a further two days. Apart from this, her recovery was uneventful.

CASE XVII.—Prolonged Unconsciousness, Possible Uræmia, Recovery—Record 784 of October 31, 1931: Mr. S., aged seventy-six years, had obstruction of a ureter and poor kidney function. He was given "Sodium amytal", 0.4 gramme (six grains), by the mouth and a hypodermic injection of morphine, 0.01 gramme (one-sixth of a grain), with hyoscine, 0.00032 gramme (one two-hundredth of a grain). Ethylene and oxygen anæsthesia was administered, while Dr. J. Close explored the kidney. A malignant mass was found to be obstructing the ureter; it was impossible to remove it, and so the wound was closed. On the following morning Dr. Close telephoned to me, saying that the man was still unconscious and that he had secreted hardly any urine. He was quite unconscious and could not be roused; his corneal reflex could not be elicited. Dr. Close considered the condition was due to the "Sodium amytal", while I diagnosed it as uræmia. However, hydrotherapy was effectual in restoring a satisfactory condition after several strenuous days. The mentality of the patient was peculiar when he left hospital.

I have since been informed by another surgeon that he treated this patient several years ago and that there were signs of uræmia and peculiar mentality at that time. Probably both Dr. Close and I were correct and that owing to the uræmia there was delay in eliminating the "Sodium amytal".

Group II.

Group II comprises complications and deaths which have no relation to the barbiturates administered.

CASE XVIII.—Secondary Hæmorrhage, Death—Record 395 of June 4, 1932: Mrs. B., aged seventy-one years, was given "Nembutal" prior to a cholecystectomy performed by

Dr. Close. Her progress was excellent until the fifteenth day, when there was a sudden profuse hæmorrhage from the wound and she died.

CASE XIX.—Post-Operative Psychosis, Recovery—Record 875 of December 7, 1931: Mrs. T., aged thirty-six years, was given "Nembutal" prior to a secondary lobectomy for exophthalmic goitre. This operation was performed by Sir Henry Newland under endotracheal nitrous oxide and oxygen anaesthesia. Parathyroid deficiency was noticed on the second day, and a few days later post-operative psychosis occurred. Her eventual recovery was good.

CASE XX.—Post-Operative Peritonitis, Death—Record 614 of September 15, 1930: Mr. M., aged nineteen years, was suffering from a faecal fistula following operations for appendix abscess and intestinal obstruction. He was very afraid of ether, as his six previous anaesthetics had been followed by very severe vomiting. "Sodium amytal", 0.58 gramme (nine grains), was administered intravenously, followed by a small amount of ether by the "open" method. The bowel was freely mobilized and the fistula closed. Peritonitis occurred with death on the second day.

CASE XXI.—Death from Shock—Record 723 of October 24, 1930: Mrs. E., aged fifty-two years, weight 81.0 kilograms (179 pounds), was given 1.0 gramme (fifteen grains) of "Sodium amytal" intravenously prior to the evacuation of a pituitary cyst. It was the intention to operate under local anaesthesia, but the patient was too restless, and ether had to be administered. Sir Henry Newland evacuated the cyst by the transfrontal route, an operation of three hours. There was considerable shock at the end of the operation. In spite of salines and other restoratives, the patient died six hours later.

CASE XXII.—Death from Shock—Record 488 of July 12, 1932: Mrs. R.S., aged twenty-nine years, had been under treatment for jaundice which developed after cholecystectomy. It had been necessary to treat her in hospital for six weeks in order to improve her condition sufficiently to allow a laparotomy. She was a thin, frail woman with very marked jaundice. "Nembutal", 0.1 gramme (one and a half grains), was given by the mouth and followed by ether by the "open" method. At the operation, performed by Dr. Rice, there was much bleeding from the separation of adhesions, and her condition steadily became worse. The ducts appeared to be normal, and no cause could be discovered for the jaundice; it was presumed to be toxic. The abdomen was closed and the patient was returned to bed with a pulse rate of 120 and systolic and diastolic blood pressures of 84 and 64 millimetres of mercury respectively. She was quite conscious one and a half hours later; but, in spite of stimulants, she became worse and died four hours after the operation.

CASE XXIII.—Death from Myocardial Failure—Record 881 of December 9, 1931: Miss A., aged sixty-seven years, had suffered from gall-stones for a number of years, but Sir Henry Newland had refused to operate on three occasions on account of her bad general condition. She was very obese, had severe myocardial disease, and her systolic blood pressure was 200 millimetres of mercury. Eventually she persuaded the surgeon to operate, and "Nembutal", 0.2 gramme (three grains), was given by mouth prior to ether anaesthesia. A cholecystectomy was performed and she was conscious half an hour after the operation was completed. Her heart gradually became worse, and she died of myocardial failure three and a half days later.

CASE XIV.—Influenza, Recovery—Record 395 of May 30, 1931: J.S., aged thirty-eight years, weight 56.6 kilograms (125 pounds), received 0.58 gramme (nine grains) of "Sodium amytal" intravenously, followed by 90.0 cubic centimetres of ether while a laparotomy was performed for the separation of adhesions. A few days later he was infected with influenza by another patient and had slight bronchitis for two days. His recovery was otherwise uneventful.

Analysis of Cases Under Review.

Barbiturates Employed.

The following barbiturates were employed in the cases under review.

"Sodium amytal", intravenously	33
"Sodium amytal", by mouth	112
"Nembutal", intravenously	13
"Nembutal", by mouth	76
"Pernocton", intravenously	10
Veronal (or barbitone), by mouth	9
"Allonal", by mouth	7
"Dial", by mouth	4
"Somnifaine", by mouth	2
"Phanadorm", by mouth	2
Total	268

Although this number is small, the cases have been investigated carefully and followed up as completely as possible. Records have been kept in all instances. Blood pressure charts were kept in all intravenous administrations and also in forty-six cases in which the drugs were given by mouth.

Anæsthesia Employed.

General anaesthesia was used in 254 cases and spinal anaesthesia in five others. An analysis of the different types of anaesthesia is as follows.

Ether, endotracheal method	107
Ether, "open" method	76
Ether, endopharyngeal method	6
Ethylene and oxygen	30
Ethylene and oxygen, endotracheal method	14
Nitrous oxide and oxygen	8
Nitrous oxide and oxygen, endotracheal method	7
Chloroform	3
C ₂ E ₂ (chloroform 2 parts, ether 3 parts)	3
Spinal anaesthesia	5
Total	259

The frequent use of ether by the endotracheal method is due to the fact that it was employed in all operations on the nose and throat and frequently in operations on the upper part of the abdomen.

Operations Performed.

An endeavour was made to compile a list of operations performed, but it had to be abandoned, as their character was so varied that eighty-five headings would have been required. However, they have been grouped in the following manner.

Abdominal operations—	
On the gall-bladder or bile ducts	19
Appendicectomy	14
Various abdominal operations	47
—	80
Operations on the tonsils, sinuses or septum	74
Thyroidectomy	7
Cerebral operations	6
Prostatectomy	6
All other operations	95
Total	268

Conclusions.

1. The barbiturates are capable of reducing fear and psychic shock.
2. The amount and concentration of the anaesthetic may be lessened by their use.
3. By their use the post-operative discomforts are much decreased.
4. The barbiturates prolong unconsciousness after operation, and this is followed by a further period during which the senses are dulled, although the patient is cooperative.
5. Local and spinal anaesthesia are assisted by the use of the barbiturates, the dose should be only

sedative, and not hypnotic, as otherwise the patient may become restless. A further advantage is that the toxicity of "Novocain" and cocaine is lessened.

6. The barbiturates should not be used as the sole anaesthetic.

7. The barbiturates should not be employed in patients who show signs of lung disease.

8. Where renal deficiency is present, the dosage of the barbiturates should be diminished.

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THE RELATIONSHIP BETWEEN ALLERGY AND ANAPHYLAXIS.

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THERE seems to be need of careful review of the information we possess on the subject of allergy, since it is obvious in various discussions during which the subject has come up, that a good deal of confusion and misconception exists in the minds of medical men.

It would appear that the best method of rendering clear the relationship and distinctions between allergy and anaphylaxis would be the recapitulation, in parallel columns or corresponding paragraphs, of the various items of knowledge we possess about each.

To deal first with anaphylaxis, it may be said that:

1. If a foreign protein be injected into a guinea-pig in a small amount, no apparent damage is done, but a change has in reality occurred and the animal is said to be in the anaphylactic state—sensitized. If, however, after a lapse of eight days, even a small amount of the same protein be injected into the same animal, the guinea-pig always reacts in the same manner and dies suddenly,

with signs of intense spasm of unstriated muscle, especially of the bronchioles, which is one form of anaphylactic shock.

2. If, by reason of the dose being reduced to almost infinitesimal proportions, the animal survives this second injection, no future injection of the same antigen can be made to induce a repetition of the anaphylactic shock—the animal is immune. Therefore, the anaphylactic state is a stage on the road to immunity.

3. If, before the administration of the second dose of the antigen, some of the blood of the injected guinea-pig be withdrawn and the serum injected into a fresh untreated guinea-pig, this second animal is found to have been sensitized to the antigen and will suffer anaphylactic shock if given an injection of the protein used to sensitize the original animal. This is called passive anaphylaxis.

4. We know that the substance produced in the treated guinea-pig by the first injection—the substance which reacts with the antigen when the latter is reintroduced into the circulation—is contained in the blood serum, as shown in the experiment of production of passive anaphylaxis. But we also know that it is contained in other tissues. For example, if the uterus of a sensitized guinea-pig be removed and be perfused with Ringer's solution until all trace of blood and serum is removed, and if it be maintained in a bath of the same solution, the addition of even a minute trace of the antigen to the bath containing the uterus will cause a violent contraction of the unstriated muscle of that organ. Therefore, the reacting substance, the reagin, is present not only in the blood serum, but in the unstriated muscle.

5. Finally, and a most important fact, it is found impossible to induce true anaphylaxis with any substance lower in the chemical scale than a protein or a colloid.

Next, let us summarize what we know of allergic phenomena in man. The corresponding paragraphs, marked 1, 2, 3, are written to allow comparison with anaphylactic phenomena.

1. Except in the case of foreign sera which do produce in man, with a single injection, a state which may be called an anaphylactic state, most of the conditions known in man as allergic manifestations are induced, not by a single exhibition of the antigen, but by a long continued series of exposures to this substance. The allergic state, therefore, seems to be produced by a long continued drain upon the bank account of tolerance in contradistinction to the sensitizing effect of a single introduction of the antigen in the case of anaphylaxis in the lower animals.

For example, the human animal frequently develops urticaria for the first time in adult life as the result of ingestion of a common food which he has eaten with impunity on numerous occasions previously. Again, a workman often first develops an eczema as the result of sensitization towards some chemical agent which he has handled without apparent injury every day for many years.

It is true that when the human animal has become sensitized toward a particular antigen, he generally reacts in the same manner and even in the same system when exposed to the influence of the same antigen. But the manifestations of allergy in man are very varied, as may be seen when we consider that spasm of the unstriated muscle of the bronchioles as in asthma, effusion of serum from small blood vessels as in urticaria, actual hemorrhages as in purpura, inflammation of the epidermis with irregular proliferation of epidermal cells accompanied by serous exudation, as in eczema, are all well recognized as allergic reactions.

Although it is true that different laboratory animals show different expressions of anaphylactic shock, it is almost invariable that any animal will respond in the same manner as any other animal of the same species. For example, all guinea-pigs rendered anaphylactic die with respiratory symptoms, all rabbits with cardio-vascular symptoms and so on. But allergy in the human subject is expressed in some as urticaria, in some as hay fever, in others as asthma, and in some as eczema.

2. Even after the actual injection of a foreign serum, as, for example, antidiphtheritic or antitetanic serum, man often behaves in a fashion very different from that which

we are accustomed to see in animals. As an illustration of this it is only necessary to recall the fact that it is not at all infrequent to observe in such cases rather severe manifestations about six days after the first and only injection. These take the form of widespread and violent urticaria, sometimes accompanied by alarming laryngeal oedema. This is sometimes explained as the result of the production of a reagin in the patient's system and the reaction of this substance with some unaltered horse serum surviving in the system after the formation of the reagin about the sixth day.

It is true that the human subject rendered anaphylactic (without the above symptoms) may, if given a second injection eight days or more after the first, show grave anaphylactic shock and even die as a result. It is also true that if a minute desensitizing dose of the antigen be given, a subsequent injection may be administered with safety—the human subject is thereafter immune to horse serum. But when we come to consider the behaviour of other allergic manifestations in man, such as asthma, urticaria, eczema, hay fever and purpura, and reactions to tuberculin or trichophyton, there is seen to be an essential difference between allergy in man and anaphylaxis in animals. This difference may be stated by saying that in allergy a single dose of the antigen, no matter whether large, moderate, or minute, will never dispel the allergic state as it dissipates the anaphylactic state. Further injections of the antigen, so far from being innocuous, as in the case of the animal which had previously been in the anaphylactic state, will always induce in the allergic human subject the usual allergic manifestation and may even intensify the sensitization.

To induce desensitization in the allergic man it is necessary to employ a long series of injections of the antigen, beginning with very minute and continuing with only very gradually increasing doses.

Therefore, allergy in man is much less clearly a stage on the road to immunity than is the anaphylactic state in animals. Also it appears that in the human subject serum sickness is much closer to anaphylaxis in animals than are asthma, urticaria, eczema, and the rest of the allergic reactions.

3. It is possible to produce passive allergic sensitization in man as it is possible to induce in an animal a state of passive anaphylaxis. On account of the danger of such an experiment in man, attempts to reproduce the phenomena of a passive allergy have been strictly limited. But the Prausnitz-Küstner experiment is an example of this transference. This phenomenon may be summarized as follows: If some few drops of serum from an allergic patient be injected intradermally into a normal individual, the skin cells in the immediate neighbourhood of the injection will, after the lapse of twenty-four hours, display a positive reaction in response to a skin test performed with the antigen to which the first subject was sensitive. This is a purely local response, however, and no response occurs in skin areas distant from the site of the injection of the serum obtained from the sensitive subject.

The problem of transference of the allergic state still requires further experiment before anything like full knowledge is available on the subject. Hitherto, transference has been demonstrated beyond cavil only when the antigen was a protein, such as egg albumen. The skin grafting experiments of Bruno Bloch to be mentioned later, though applicable to a cognate problem, are not conclusive to this particular phase of the question.

4. As mentioned in the preceding section, the Prausnitz-Küstner reaction demonstrates that the serum of a human subject suffering from an allergic sensitiveness manifesting itself as a skin reaction (such as urticaria or eczema) contains reagin which, on injection into a normal individual, fixes itself on nearby skin cells. As a result of this, these skin cells give a positive response to a test made with the antigen. Therefore, as in anaphylaxis proper, the reagin is not confined to a single tissue.

More than this, the reagin, once established in the cells of a particular tissue, as, for example, the skin, remains there for a very long time. Even if the tissue is removed from the sensitive individual and grafted upon another non-sensitive person, the reagin remains potent.

This is shown by the crucial experiments of Bruno Bloch.⁽¹⁾ Bloch had infected himself with ringworm and showed a regular positive response to an intradermal test with trichophyton. He used some of his own skin to graft an ulcer in a non-sensitive person. When the graft took and the ulcer had healed, repeated tests with trichophyton gave positive results in the cells of the skin graft, but gave no results in the patient's own skin. Exactly the same results followed when the skin of a person acutely sensitive to iodoform was used in grafting an ulcer in a non-sensitive subject. Skin tests with iodoform produced strong positive reaction in the graft, but none in the skin of the host. There is, however, no record of the serum of the subject who was sensitive to iodoform having rendered the skin cells of a normal person sensitive when injected in the manner of the Prausnitz-Küstner experiment. Therefore, the proof of transference of allergic sensitization to a non-protein substance is still lacking. In allergy, then, as in anaphylaxis, the reagin is present not only in the serum, but in the cells of other tissues as well. It is probable that allergic sensitization can be transferred to another individual, as in the case of passive anaphylaxis, but so far definite proof of this transfer is available only when the antigen is a protein.

5. Although the antigens in many of the allergic reactions in man are proteins, there are many examples of allergic sensitization toward substances of chemical composition much lower than protein. Especially is this the case with many of the antigens which determine eczema, and to a less degree with those that cause urticaria. As an illustration, urticaria has often been observed as a result of the ingestion of substances like quinine and aspirin, and eczema may be the result of sensitization to much simpler substances, like perchloride of mercury, or even an element like sulphur.

Carbolic acid or iodoform, applied externally, and "Salvarsan", given intravenously, are known as causes of eczema. Such substances are, of course, quite incapable of causing the anaphylactic state in animals. Moreover, in such well recognized allergic manifestations as dermatitis from poisoning with *Rhus toxicodendron* (American poison-ivy) and dermatitis due to *Primula obconica*, it has been shown quite definitely that the substance to which the sufferer is sensitized is not the protein of the plant, but a glucoside.⁽²⁾⁽³⁾

When we come, then, to a consideration of allergic manifestations and correlate our findings in this with the results of laboratory experiments on the production and phenomena of anaphylaxis in animals, we are faced with facts which show that, though the anaphylactic and the allergic states are closely related, there are certain very definite distinctions. It seems probable that serum sickness in man is true anaphylaxis, since it is induced by a single injection of a protein antigen and may be entirely dissipated by a second minute injection of that substance.

But in by far the greater number of instances of allergic sensitization in man, for example, in asthma, urticaria, eczema, hay fever, a long continued series of exposures to the antigen is necessary to exhaust the stock of tolerance possessed by the subject. This stock of tolerance once exhausted, the patient is allergic.

Again, the allergic state cannot be dissipated by means of a single injection of a minute amount of the antigen. Yet this always succeeds in anaphylaxis (if the dose given is insufficient to kill the animal). On the contrary, in allergy it is necessary to give a long series of minute amounts of the antigen to desensitize the patient and this desensitization is often only temporary, though desensitization in anaphylaxis is always permanent.

A third and most important difference between allergy and anaphylaxis is that the anaphylactic state can be induced only by using a protein or colloid antigen, while the allergic state may be due to sensitization toward an antigen of a much simpler chemical structure.

This last point has attracted by far the most attention from laboratory workers, and to eliminate this apparently crucial difference, it has frequently been suggested that the simple chemical agent combines with the patient's own proteins and that the resultant compound is the real antigen. This is not easy to reconcile with the facts in the case of rhus and primula poisoning caused by glucosides which exist in the plant without combining with the proteins of the plant and which must yet be supposed to combine with human proteins.

Moreover, this is not the only difficulty in the way of making allergy a variety of anaphylaxis. The differences in the manner of induction and of dissipation of the two states are also very important, if not crucial.

Therefore, it is to be suggested that, instead of attempting to describe allergy as a variety of anaphylaxis, instead of trying to crowd allergy into the mould of anaphylaxis, it would be better, as Bloch points out, to regard anaphylaxis as a very special variety of allergy, a variety which can be produced only by the use of a protein antigen.

Common Allergic Manifestations in Man.

Three main types of allergic reaction exist. One is that depending upon changes in the cardiovascular system. Examples of this are: (i) urticaria, in which there is increased permeability of the fine blood vessels allowing a rapid exudation of serum; (ii) purpuric eruptions, in which there is allowed extravasation of whole blood.

A corresponding type of anaphylactic shock is found in the rabbit which dies as a result of profound lowering of the blood pressure due to dilatation of the blood vessels, especially in the splanchnic area.

A second variety of allergic manifestation is that in which there is spasm of the unstriated muscle, especially in the bronchioles. An example of this is asthma, in which, however, there is local exudation and some cellular reaction as well.

The third main variety is that in which the reaction is mainly cellular. The typical example of this is eczema, in which the cells of the protoplasmic layer of the epidermis become swollen and cloudy and in which irregular reproduction and imperfect keratinization occur if the irritant continues in operation. There is an accompanying vascular fault, which is expressed by dilatation causing erythema, and by increased permeability causing serous exudation, oedema and vesiculation.

In hay fever the main feature is a vascular one, causing exudation, shown in oedema of the mucous membrane, but there is increased cellular stimulation, as shown in the greatly increased secretion and irregular proliferation of the cells of the mucous membrane.

Finally, there is the variety expressed in a positive response to the application of tuberculin or trichophytin to an abrasion of the skin. Here what we regard as a manifestation of disease in the case of urticaria and eczema is expressed as a physical sign. The erythema and œdema of a positive von Pirquet reaction are exactly the same as the erythema and œdema produced by an intradermal test with linseed in an asthmatic who has become sensitive to that substance, and are identical with the redness of an eczema in a laboratory worker who has become sensitized toward formalin.

When an infant is new-born, a von Pirquet test calls forth no response because the child has not become sensitized by infection. When once infection with tubercle bacilli has occurred, provided the infection is resisted by the natural or developed forces of the subject, the application of tuberculin will bring into conflict the antibody or reagine produced in the patient by the previous infection. The signs of the conflict are mainly vascular, namely, dilatation and exudation.

When no resistance or very little resistance is offered to the infection by the victim, as, for example, when a first inoculation with tubercle bacilli induces an acute miliary tuberculosis, or when the natural resistance to the infection is finally worn down, as in a terminal miliary tuberculosis, the von Pirquet test calls forth no response.

Therefore, a positive response to a von Pirquet test is an expression of resistance to the infection and has elements of hope in it which an absence of response in the presence of a known infection does not possess. As all who have arrived at adult life have had numerous inoculations with tubercle bacilli which have been overcome or held dormant, most people may be expected to show some degree of positive reaction to a tuberculin test.

Trichophytin is a similar substance made from pulverized ringworm fungus. If a deep ringworm infection has occurred, the patient will for many years afterwards give a positive response to a test performed with this extract.

Certain other phenomena accompany resistance to tuberculosis and incidentally to leprosy and other infections. These are cellular responses. In a well resisted but not entirely vanquished tuberculosis or leprosy the formation of giant cells and the arrangement of these cells with epithelioid cells and lymphoid cells in follicular fashion may be regarded as allergic manifestations.

The tendency to react in an allergic fashion is an hereditary one. The family mentioned by Osler, in which, during three generations, there were twenty-two members who suffered from giant urticaria, is an illustration of this. It is not, however, to be understood that giant urticaria is an hereditary disease, because it is now found that many families exist in which, though the progenitor suffered from asthma, for example, the descendants have manifested their allergic inheritance, some in the form of urticaria, some as asthma and some as eczema.

The inheritance is, then, a susceptibility to become sensitized and accident probably determines in which system and in what manner the sensitization is manifested.⁽⁴⁾

Another inherited characteristic may be a potent factor in determining sensitization to external irritants. Ichthyosis and its minor relative, xeroderma, are transmitted from parent to child (though not necessarily to all offspring or in the same degree). In these conditions the horny layer is not supplied with enough grease to act as an efficient waterproof covering and therefore the deeper protoplasmic layers of the skin are rendered more easily accessible to potential antigens soluble in water. As a result of this fault tolerance is exhausted earlier than with a person possessed of a normally waterproofed horny layer. Conversely, in munition workers, eczema due to sensitization toward trinitro-toluol (soluble in grease) was more common in those who had greasy (seborrhœic) skins.

The most important diseases known to be allergic in origin are asthma, eczema, urticaria, hay fever and purpura. There are possibly others, but these need not be considered at the present juncture. For example, the toxins and products of many bacteria may act as antigens and induce allergic response in man. But an attempt to cover all these would require much more space than is at present available, and therefore I am compelled to restrict illustration to two diseases of the skin, urticaria and eczema.

Urticaria.

Urticaria is perhaps the best example of allergic disease, because urticaria and exudation are two of the most prominent features of true anaphylaxis in man, as shown in serum sickness.

There are three main varieties of urticaria occurring as natural phenomena. These are giant urticaria, common urticaria and papular urticaria of children.

Giant Urticaria.—In giant urticaria the effusion of serum is profuse and causes swelling as big as an egg or even as an orange. An eyelid may swell until it completely closes the eye with a swelling as big as an egg. The lip may swell to three or four times its natural size. The tongue may protrude from the mouth, or a lump as big as an orange may appear on the hand. Several or many such swellings may occur at the same time, and their development takes only a few minutes. These are very alarming to the patient and when, as sometimes occurs, they involve the mucous membranes, they are frightfully dangerous, causing death in some cases by occlusion of the larynx if intubation or tracheotomy is not performed. The terror engendered in a patient who has once or several times experienced the near occlusion of his respiratory passages is easy to understand, but this terror was responsible for the former use of the now obsolete name for this condition—angio-neurotic œdema. The œdema is now known not to be due to a neurosis, but the neurosis to the œdema.

Giant urticaria is fortunately not a common condition, but when it occurs it constitutes a major emergency which every practitioner must be prepared to face with knowledge and calm preparedness. It is necessary to dismiss the idea of neurosis from the mind, get out the intubation and tracheotomy set and to sit by the patient fully prepared to use them. A good saline purgative should be administered and the patient should be starved altogether unless it is perfectly certain he is not sensitive to milk. After the starvation, milk and water only should be allowed for another twenty-four hours. From this add, item by item, different foods until another attack occurs, when the latest addition is obviously the cause. Thereafter the offending food is to be rigidly avoided.

During the attack adrenaline (0.3 mil or five minims of the one in 1,000 solution) should be injected and repeated every hour, or even every half hour, as often as seems to be required. The vaso-constrictor effect thus obtained is most valuable in the exudation period, but is, of course, very temporary. The attack often lasts about twenty-four hours, but the dangerous peak period is generally only an hour or two in duration, unless the antigen is again administered. Hence the importance of starvation unless the antigen is already known.

Giant urticaria has been known within the writer's experience to be due to therapeutic serum (probably true anaphylaxis), to aspirin, to prawns, and to tomato. Many other antigens have been found responsible, and nothing is to be regarded as above suspicion.

Scratch or abrasion tests with various foods should be done to enable safe additions to be made to the diet and to discover the cause and thereby avoid the risk of another attack.

Desensitization may be attempted, but generally the simplest way is rigidly to exclude the offending food from the diet. This is easily obtained by reason of the terror inspired in the patient by the antecedent attack.

Common Urticaria.—In common urticaria the exudation of serum is nothing like so profuse in any individual lesion, though the wheals may be very numerous and the itching may be maddening. This type also occurs in serum sickness, and the severity of the itching may demand the use of morphine. Except when it is a manifestation of true anaphylaxis (serum sickness), it never affects the mucous membranes, and is, therefore, not dangerous. But the patient would generally prefer to have an acute appendicitis, undergo an operation and be done with it, than suffer the recurring agonies of itching which the urticaria of unsolved origin occasions. Adrenaline helps, but not very much in most cases, and has to be pushed to the utmost limit of safety if full relief is aimed at. A smart saline purge, a day's starvation, and the gradual addition of food, item by item, to the diet is generally the best plan.

If the urticaria is a daily occurrence, obviously it is a common food that is to blame. The antigen, therefore, must be looked for among the articles like bread, milk, butter, meats and vegetables, and fruits, jams and even honey must not be forgotten. If attacks are spaced with intervals of freedom amounting to several days or weeks, an occasional food is suspect. The cause might be a fruit, an unusual vegetable, a meat like pork, or shell fish like prawns or lobster. Quinine and aspirin are known to have been responsible. And it should be borne in mind that a leaking hydatid cyst will cause urticaria.

Abrasion tests or intradermal tests may help, but often so many tests may have to be applied that the process becomes too tedious or too expensive.

When the cause is discovered, if the antigen is an uncommon food or a drug, eliminate it. If it is a common food, like wheat flour, it may be necessary to attempt desensitization.

Papular Urticaria of Children, Lichen Urticatus, Strophulus.—In papular urticaria of children the wheals are like insect bites, small and dome-shaped, and are soon scratched, so that they are capped with blood crust. There are areas of major concentration, lesions being thickest on the lower legs, next on thighs and buttocks, while a few may occur on forearms and even on the face in very severe cases.

In this variety it is almost always a food that is responsible, sometimes a common food like wheat or oatmeal or egg, and even milk. Generally the child's diet is ill-balanced and the body ill-nourished. There may be several antigens responsible. Fruits are commonly to blame, especially strawberries in countries where there is a season of abundant cheap berries. But anything in the child's food supply may be the actual cause, and all items should be suspect.

Again a diet with gradual additions is generally necessary, but with an anxious mother and a fractious child a day's starvation is generally impracticable. It is frequently necessary to put the patient in hospital away from the mother in order to obtain a solution of the problem. If the child is not in hospital, the mother must keep in a notebook an absolutely accurate record of every atom of food and drink the child has, and on the opposite page enter the time of the appearance of every fresh crop of lesions. Skin tests are rarely satisfactory.

Desensitization may be attempted if the antigen is contained in a common food like wheat or milk, but is very difficult to carry out satisfactorily. If wheat is to blame, biscuits and cakes made of oatmeal can be used. If a fruit is responsible, it is best to cut it out, together with jams and conserves of the fruit.

Eczema.

Eczema is the next example, and as the appearance and stages of this disease are already familiar, it is not necessary to repeat them here. But it is

necessary to draw attention to the fact that seborrhœic dermatitis, septic and epidermophyton infections which cause "eczematoid" lesions, are to be excluded from the group of manifestations known as eczema. Also it is necessary to point out that, unlike urticaria, which is always due to the ingestion or the injection of the antigen, eczema is almost always caused by an irritant acting locally, that is, upon the skin from outside.

It is true that in not a few infantile eczemas a food is to blame, and it is also true that sensitization, for example, to arseno-benzol administered intravenously, may result in an eczematous eruption, but it is only very rarely that the eczema of the adult is due to a food or drug.

Again, eczema is the example *par excellence* of the effect of the gradual exhaustion of the bank account of tolerance. It is common to find that a workman, after having been able to handle with impunity for many years a particular chemical substance, will suddenly become intolerant and thereafter develop an eczematous attack whenever this substance comes into contact with his skin.

Eczema, too, provides the best example of sensitization toward simple chemical substances. Mercurial salts, simple sulphur, carbolic derivatives, any antiseptics, like formalin and "Eusol", for instance, simple cleansing agents, as well as essential oils like eucalyptus or the derivatives and juices of different plants, almost anything up and down the chemical scale, things innocuous to everybody except the thousandth individual, may act as antigens in the production of eczema.

It is this very multiplicity and reputed innocuousness of a great many of the possible causes of eczema that provides the greatest difficulty in solving the problem of the causation in the individual case, and of convincing the patient that the trusted carbolic soap which he and his family have used for years, is in reality responsible for his trouble.

The interdiction of all antiseptics and active chemical substances, including soap, is the first thing to do. When the skin, under suitable inert protective dressings has returned to normal in appearance, gradual relaxation of the rule is permitted until a fresh attack occurs, when the cause should be obvious even to the patient.

When one has a suspicion or an inkling by reason of the man's trade that a particular substance is to blame, patch tests are very valuable, especially to convince the patient, or to prove to a court that his eczema is an occupational one. When a patch made of a particular substance produces in twenty-four hours a red œdematous patch that stings and itches and may even weep, the patient can see and feel that the substance applied by the patch had best be avoided.

Desensitization, when necessary, can rarely be done by specific antigens. Often auto-hæmotherapy greatly reduces sensitiveness. Small doses of X rays probably act as a physical desensitizing agent. But as a rule avoidance of the cause is possible and should be insisted upon.

Asthma.

Another very important example in asthma had best be left to one more familiar with its vagaries. But the behaviour and causation of asthma do no differ in essence from the examples already given.

It is hoped that this *résumé* of our knowledge of allergy, as manifested in everyday medicine, may be of use in clarifying the ideas of practitioners and in affording a lead as to the choice of therapeutic measures.

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OIL OF AUSTRALIAN SANDALWOOD.

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THE "British Pharmacopœia, 1932" contains an addition of particular interest to Western Australia. This is oil of Australian sandalwood (*Oleum Santali Australiensis*), derived from *Eucarya spicata* Sprague and Summerhayes (synonyms, *Fusanus spicatus* R. Brown, *Santalum spicatum* A. P. De Candolle, *Santalum cygnorum* F. A. W. Miquel). The plant is known as the fragrant or Swan River or Western Australian sandalwood, of the family Santalaceæ. It is essentially a Western Australian species, growing on areas of low rainfall, but extends to northern and eastern Australia, including Queensland. The essential oil is distilled from the heart-wood and rectified. It is obtained from the butt and roots as well. The pharmacopœia describes it as distilled from the wood. Oil of Australian sandalwood closely resembles the ordinary oil of sandalwood, obtained from *Santalum album* Linné, which is indigenous to southern India and the East Indian Islands, but is cultivated in other parts of tropical Asia. Madras produced the oil, but it is now practically a monopoly of the Mysore Government in India. Mr. A. R. Penfold, Curator and Economic Chemist, Sydney Technological Museum, has made extensive investigations into the Australian oil, which contains up to 95% of alcohols. Whether these are identical with the santalols of ordinary sandalwood oil of Madras and the East Indies has been a matter of much controversy. Early samples of Australian oil contained only 75% of sesquiterpene alcohols. In its crude condition East Indian oil contains about 90% of sesquiterpene alcohols and small amounts of other alcohols, but, according to Mr. Penfold, it is considered to consist essentially of the sesquiterpene

alcohols, α - and β -santalol. Western Australian oil contains about 60% of santalol, the remainder consisting of a very closely allied sesquiterpene alcohol. The pharmacopœia requires that Australian oil shall contain not less than 90% weight for weight of free alcohols, calculated as $C_{15}H_{24}O$. The limits of optical rotation are -3° to -10° . Ordinary oil of sandalwood (*Oleum Santali*) is the oil distilled from the dried heart-wood of *Santalum album*, containing not less than 2% weight for weight of esters, calculated as santalyl acetate, and not less than 90% weight for weight of free alcohols, calculated as santalol, $C_{15}H_{24}O$. The optical rotation is -15° to -20° (at 20° C.). The dose of the Australian oil is five to fifteen minims (approximately 0.3 to 1.0 mil). It is of excellent quality and the equal of any other for therapeutic purposes. It has been in medicinal use for some years. It has a more fragrant odour than the Madras oil, resembling in that respect oil of the Fiji species (*Santalum yasi* Seemann). The wood is largely exported to China, Hong-Kong and the Straits Settlements for use as incense and in carving. Large quantities of the oil are exported to America for use in the soap industry.

This remarkable plant, which attains the magnitude of a small tree, is a root parasite, hence the difficulty of transplanting it. All attempts at its reproduction on a commercial scale have been futile. Large tracts of forest have been denuded of sandalwood, which has been shipped from Western Australian seaports to Eastern markets. Within two hundred and fifty miles of Perth most of it has been removed. The demand for it is so great that, whenever seen, it is torn up by the roots ("Australian Encyclopædia"). According to H. V. Marr, the sandalwood industry in Western Australia dates back to 1846, when four tons of wood, valued at £50, were exported. In recent years the best quality has been cut from an area including Kalgoorlie, Kanowna, Laverton and Mount Morgan districts. Up to 1922 exports of sandalwood from Western Australia amounted to over 350,000 tons, valued at nearly £3,300,000. As regards the oil itself, the production has increased from 6,870 pounds weight in 1921 to about 100,000 pounds in 1930.

Santalum freycinetianum Gaudin and *Santalum pyrrularium* A. Gray of the Sandwich Islands also yield sandalwood. An Australian species, *Santalum lanceolatum* R. Brown, known as sandalwood or the blacks' medicine tree, extends from Western Australia to the interior of New South Wales, and occurs abundantly in Queensland. It yields a sandalwood of an inferior odour. The fruit was eaten by the aborigines about the Gulf of Carpentaria, and the bark, steeped in water, was used by the natives of the interior of New South Wales for medicinal purposes. According to Mr. Penfold, the oil of this species contains 90% of a sesquiterpene alcohol, $C_{15}H_{24}O$. It is highly lævo-rotatory, with an optical rotation of -66.7° and yields a beautiful, well defined crystalline allophanate with

a melting point of 114° . The boiling point of the alcohol is 153° to 154° (three millimetres). The specific gravity is 0.9474. The refractive index at 20° is 1.5074. The oil was, to a certain extent, employed by Western Australian manufacturers to bring up the lævo-rotation of the oil of *Eucarya spicata*, but this use is not now continued. The oil of this species is not now in use, but large amounts of the wood are exported to the East for making incense. Probably the oil could be used for purposes similar to those of the other sandalwood oils. Other Australian species, such as *Santalum obtusifolium* R. Brown and *Santalum ovatum*, yield sandalwood of inferior odour.

Fusanus acuminatus R. Brown (synonym, *Santalum acuminatum* A. De Candolle) is the well known quandong or native peach. The white kernel of the "seed" (or stone) is very rich in oil and palatable for eating, resembling in taste a peach kernel. Both fruit and kernel were eaten by the blacks and the bark was used for tanning skins. *Fusants persicarius* F. von Mueller (synonym, *Santalum persicarium*) is a small tree extending in habitat to New South Wales. It furnishes a sort of sandalwood. The roots, nutritious but tasteless, were used by the aborigines, after roasting in hot ashes, as an article of diet.

Reports of Cases.

AN EARLY DIAGNOSIS OF ANTHRAX INFECTION.

By A. J. CUNNINGHAM, M.D. (Sydney),

Honorary Assistant Gynaecologist, Sydney Hospital.

ON May 25, 1932, a young man, aged twenty years, consulted me with regard to tenderness and swelling of the fifth digit of his right hand. The history was that he had been working in a brush factory at Bondi, and, owing to competition with firms in Adelaide, his employer had decided to make softer haired brushes, and two days previously (May 23, 1932) he had started working on sheep skins and goat skins.

On examination, he had a tender, œdematous and red fifth right finger. There was a tiny black spot the size of a pin head on the lateral and dorsal aspect of the first knuckle. There was marked lymphangitis of the arm, with lymphadenitis at the elbow and axilla. The temperature was 37.8° C. (100° F.), the pulse rate was 110. He said he felt ill. On the next morning his finger was slightly more swollen and he gave the history of "having red streaks up the back of both legs". These, he said, disappeared and reappeared from time to time. On examination of his legs he had lymphangitis on the posterior aspect of the right thigh. In view of this history and the somewhat abnormal clinical signs of the infection he was sent to the Pathological Department of Sydney Hospital, where some serum was obtained from beneath the skin at the site of the first knuckle of the little finger. This was stained, and microscopical examination showed small clumps of anthrax bacilli. He was treated by a cross incision into the little finger and application of pure carbolic acid and anthrax antiserum. This was given intravenously and subcutaneously for three days. He made an uninterrupted recovery, except for serum sickness on the tenth day.

I consider this case interesting and worthy of report for the following three reasons: (i) The rarity of the condition, (ii) the diagnosis before the appearance of a typical malignant pustule, (iii) the success of the large doses of serum without excision.

A CYST OF THE IRIS LOOSE IN THE ANTERIOR CHAMBER.

By J. BROOK LEWIS, M.B., B.S.,

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H.K., A FEMALE, aged thirty-six years, complained that for the previous six years she had noticed a small body moving about in the right eye, and that occasionally it interfered with her vision, but if the eye was rubbed the obstruction disappeared. During the previous week she had suffered a lot from pain in the right supraorbital and infraorbital regions.

There was a history of an attack of trachoma thirteen years previously. At that time she had an ulcer in the right eye.

The vision in each eye was $\frac{6}{12}$. There was some old scarring in the lids, and there were some vessels in the top of the cornea of the right eye, together with an old corneal scar. In the bottom of the right anterior chamber there was a small black object, three millimetres in diameter, as measured through the cornea. By rubbing the eye or altering the position of the head the body could be moved to any part of the anterior chamber. Examination with a slit lamp showed it to be a biconvex translucent sphere with pigmented walls veined with thicker tissue. At the pupillary margin of the right eye there was a splitting of the pigment layer at six and twelve o'clock. The iris stroma at twelve o'clock showed a vertical pigment streak about one millimetre long.

A keratome incision was made in the upper part of the limbus and the cyst was washed out with the aqueous humour and crushed by lid action. In its collapsed condition it measured one millimetre across. Dr. Bull reported it to be a retention cyst of the iris.

Reviews.

ENTOMOLOGY.

"RECENT ADVANCES IN ENTOMOLOGY", by A. D. Imms, brings together in an attractive and convenient form all the more striking advances made in entomology during the last decade, both in the field of pure morphology and in its more applied aspects.¹ To those other than systematists, the latter chapters of the book, and particularly those dealing with ecology, parasitism and biological control, are of greatest interest. Nevertheless there is much in the chapters dealing with sense organs and reflex behaviour which should be read by physiologists, while the chapter dealing with fundamental aspects of coloration has a real bearing on certain problems of genetics. It is, however, in the field of ecological investigation that those other than entomologists will find most entertainment; and there is abundant interest for any reader in the consideration of the effects of temperature, humidity, light, food and climate on the development and survival of the more important economic species.

For example, in relation to the depredations of the Mediterranean fruit fly, *Ceratitis capitata*, investigation has shown that these are practically limited to those

areas which lie almost entirely between the January isotherms of 10° in the two hemispheres, and it is in the still uninvaded areas lying within these boundaries that the introduction of this pest constitutes a very real danger.

In Chapter X, dealing with the practical application of ecology, a very interesting illustration is given of the manner whereby losses from the fruit fly of oats may be decreased by sowing crops slightly earlier, so that they will have reached a resistant stage before the parasite has attained its greatest seasonal increase, while equally striking is the evidence that cultural methods, by altering the nutritive properties of cereal crops, will also tend to lessen the harmful effects of the parasites upon them; thus manuring with superphosphate will definitely diminish the harmful effect of the gout fly of barley.

To come to an Australian illustration, we have the possible influence of an increase in the pH of soil, by cultivation or rainfall, in lowering the incidence of the springtail, *Sminthurus viridis*.

Of particular interest to Australians is the convenient summary of the present state of knowledge in regard to the phenomenon of biological control. It is rather discouraging to find that, in the opinion of the author, biological control has achieved and will continue to achieve its most striking results in island masses or in areas which for topographical or climatic reasons constitute a definite and limited unity. In the light of this we cannot be too sanguine of biological control achieving the results expected of it in the control of the blow-fly in Australia, or in checking the spread of that still largely potential menace, the buffalo-fly.

Only one small typographical slip has been noted, and that is the placing of the Ipswich fossil beds in New South Wales, instead of in Queensland, on page 78.

Not the least satisfactory feature of this book is its admirable documentation, a list of references being conveniently given at the end of each chapter. It is a book which in many ways is as interesting to the professional man in general as it is essential to all those who are directly concerned in the advances of this very important branch of scientific knowledge.

EPIDEMIC ENCEPHALITIS.

A LITTLE more than two years ago we had pleasure in calling attention to the very useful work which had been carried out by the Matheson Commission in epitomizing the literature on epidemic encephalitis. Since the publication of this survey in 1929, a large amount of further investigational work has been carried out on this disease. Many publications in various languages deal with this subject. In a "Second Report" these various works are succinctly epitomized¹ and the inquirer is thus given an indication of the scope of an article, to which he can then refer should fuller details be desired. The first chapter deals with works on the aetiology of the disease. Authorities are still divided as to the nature of the causative agent. Some consider it to be the same as the herpetic virus; others consider that it is an allied virus specifically distinct from that of *herpes simplex*; some even hazard the possibility that the causative agent may be something midway between a ferment and a living entity. Chapter II deals with other types of encephalitis, including post-vaccinal encephalitis, and here again opinion is divided. Chapter III deals with the treatment, showing that many drugs have been tried, but, as might be expected, with results only too often uncertain. The chapter on epidemiology is followed by a full bibliography.

We note with deep regret the sudden death of Dr. William J. Matheson, whose generosity made the work possible. We trust that the work he started may continue its successful course.

¹ "Recent Advances in Entomology", by A. D. Imms, M.A., D.Sc., F.R.S.; 1931. London: J. and A. Churchill. Demy 8vo., pp. 352, with 84 illustrations. Price: 12s. 6d. net.

¹ "Epidemic Encephalitis, Etiology, Epidemiology, Treatment", Second Report by the Matheson Commission, 1932. New York: Columbia University Press. Crown 8vo., pp. 155. Price: \$1.50 net.

The Medical Journal of Australia

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HÆMATURIA.

WHEN a patient consults a medical practitioner regarding a symptom or a combination of symptoms which has caused pain or discomfort or uneasiness of mind, he expects that the practitioner will make every effort to discover the cause of the symptoms and will order appropriate treatment. The symptoms are often caused by an infection or by a pathological lesion which is obvious, and in these circumstances the treatment will not be difficult. Sometimes the cause of the symptoms is obscure, but the anxiety of the patient is on this account no less acute. Sometimes, though rarely, the patient's anxiety has foundation neither in bacterial infection nor in other pathological condition—the patient is suffering from a neurosis. The word “rarely” needs emphasis, for the more erudite and skilful the practitioner, the more seldom will he make a diagnosis of neurosis. All medical practitioners can call to mind cases in which they have, perhaps reluctantly, ascribed the patient's illness to a nervous system susceptible to impressions and prone to exaggerate trifles until they dominate the whole mental outlook; later on, something has happened; perhaps signs of irretrievable damage have appeared and there has come a realization that, had the search been more diligent, had the weighing of evidence been more impartial, disaster might

have been averted. It is, of course, the duty of every medical practitioner to allay the fears of his patients; he generally does what he can to allay fear in the full knowledge of his patient's bodily condition and while he applies appropriate treatment. The battle is often half won when the patient has made up his mind that he will recover. Whatever may be thought of a patient's subjective symptoms, to make light of his condition in the presence of objective signs, which should be regarded as of serious import, is, to say the least of it, reprehensible. One of the signs most frequently disregarded is hæmaturia.

Hæmaturia may arise from many causes. It may be caused by lesions of the genito-urinary tract and also by systemic diseases and by lesions in structures adjacent to the genito-urinary tract. When it is the result of direct continuity of lesions in adjacent organs, such as the appendix, ovary and gall-bladder, there will be no great difficulty in diagnosis. Hæmaturia in blood dyscrasias—hæmophilia, purpura, scurvy and the like—will be easily traced to its origin. Likewise, hæmaturia due to infective fevers or to drugs such as cantharides and turpentine will present little difficulty. Lesions of the genito-urinary tract likely to cause hæmaturia are those of the kidney, ureter, bladder, urethra and prostate—in other words, any portion of the tract may be responsible. Most difficulty will be experienced with lesions of the upper portion of the tract. Mackenzie analysed 821 cases in which hæmaturia, due to causes in the upper part of the tract, was sufficiently severe to attract the attention of the patient. Calculi were responsible in 192 cases, tumours in 113, renal tuberculosis in 88, and surgical infections of the ureters and kidney in 143. The number of tumours in this series was large, and tumours more than any other condition are likely to give rise to “symptomless” hæmaturia. Cases not uncommonly occur in which a patient has complained of passing blood in the urine, examination by ordinary clinical methods has failed to reveal a cause for the bleeding, the bleeding has stopped and the patient has been assured that there is “nothing to worry about”.

What must be remembered is that there is no such thing as “essential hæmaturia”. Hæmaturia

always has a cause, and it is the duty of the medical practitioner to discover the cause. While all practitioners will agree with this statement, they will not all put it into practice. It is astounding how many will succumb to the wish of an anxious patient to be assured that there is no cause for alarm. There need be no hesitation in sending a patient for expert examination by a urologist or by a radiologist or by both. Cystoscopy, pyelography and excretion urography have been brought to a state almost of perfection, and those skilled in their use will seldom fail to discover such a lesion as a tumour of the kidney. We cannot do better than reiterate some of the conclusions recently stated by Dr. M. S. S. Earlam in this journal:

1. The majority of cases of hæmaturia require cystoscopic investigation for their complete diagnosis.

2. All patients with symptomless hæmaturia, without obvious basis, must be regarded as suffering from neoplasm until the contrary is proved.

3. Though what appears to be the primary cause of an infective hæmaturia may be suggested by clinical examination, it is not safe to regard it as such unless both the hæmaturia and pyuria clear up completely under treatment.

Hæmaturia is never a condition to be dismissed as of no account.

Current Comment.

MICROCYTIC ANÆMIA.

THE remarkable results obtained by liver feeding in true pernicious anæmia have aroused such interest and optimism in the handling of patients suffering from various types of blood deficiency that there is some danger that the value of certain simple drugs, like the inorganic preparations of iron, may be forgotten. The natural tendency of the clinician when confronted with an anæmic patient, is to prescribe liver or desiccated stomach in some form, even though he well knows that he is not dealing with the anæmia for which such treatment is specific. It is curious to reflect that the application of liver therapy to pernicious anæmia by Minot and Murphy was based on Whipple's work on post-hæmorrhagic anæmia, and it has since been the experience of physicians that liver, though of value in some secondary types of anæmia, does not evoke a dramatic response comparable with that seen in the Addisonian disease.

Douglas Vanderhoof and Dewey Davis, in a recent communication, report five cases of a type of anæmia that is being described more frequently of late, a chronic deficiency of both blood cells and hæmoglobin, occurring in middle-aged women.¹

Though these patients had achlorhydria, and four out of five had atrophic tongues, their blood picture was quite distinct from that seen in pernicious anæmia. The red cells were on the average smaller than normal, and the colour index was low. There was a history of excessive menstrual bleeding in every case, but this could not have been the only factor involved, for no similar reduction in the size of the erythrocytes was observed in women suffering from anæmia secondary to uterine bleeding. Nor did men who were the subjects of achlorhydria display any such change in their blood. Witts and others have drawn attention to this particular morbid state of the blood, which apparently is a more or less definite disease entity. Their experience has been that the administration of iron has given quite satisfactory results, and this tallies with the observations of the present authors, who have also tried to evaluate the effect of liver feeding. Vanderhoof and Davis found that whole liver was quite effective in producing blood regeneration and that an aqueous extract possessed identical properties. Although their series of cases is but a small one, this finding is of interest. The patients were also given hydrochloric acid. It is also pointed out by Vanderhoof and Davis that appropriate treatment for the uterine bleeding is of great importance.

The interest of this article lies in the recognition of a variety of anæmia that must be not at all uncommon and that is extremely easy to treat. It is, of course, of immense importance that two diseases be excluded from the clinical diagnosis in these patients near the menopausal age, pernicious anæmia and carcinoma of the uterus or other organ. Once this is done, the practitioner can confidently look forward to relieving his patient with reasonable speed and certainty. Inorganic iron, as has been pointed out in these pages recently, is more effective than the organic form; it is not expensive, and is usually taken more easily than liver. Remembering that an adequate dose should be given (and this is as a rule greater than the official pharmacopœial dose) and that relapse is likely to occur unless medication is maintained over a prolonged period, a good result should be obtained. It is probable that, could we call in consultation a physician of a couple of generations ago, he would be much interested in the modern pathological and biochemical findings, but would dryly observe that the treatment was exactly the same as his own, which had always yielded most gratifying results both to himself and his patients.

THE TOXIC ACTION OF THE CINCHOPHEN DRUGS.

ATTENTION has been directed on many occasions to the toxic potentialities of the drugs of the cinchophen group, best known to the lay and professional public in the form of several proprietary preparations, such as "Atophan". Three years ago, J. D. Maude and S. O. Cowen both made communi-

¹ *The American Journal of the Medical Sciences.*

cations on this subject to this journal. Dr. Maude pointed out that in the years 1926 and 1927 the deaths certified as due to acute yellow atrophy of the liver were more than double those of previous years, and both he and Dr. Cowen drew attention to the danger of uncontrolled sale of these drugs. Although danger from this source has been denied, there seems to be little doubt that prolonged administration of such preparations does at times cause hepatic damage, and even correct dosage over a limited period may give rise to poisonous symptoms. This need not exclude the drug as too dangerous to use, for there are no potent drugs that produce no toxic symptoms, even if such symptoms are rare, and idiosyncrasies to even the most harmless of pharmacopœical preparations are not uncommon.

H. B. Myers and L. Goodman have contributed to the experimental study of this subject and record their work on dogs and rabbits to which cinchophen was administered either in enteric capsules or admixed with the food.¹ Rabbits appear to be less susceptible than dogs, and were given ten times the calculated therapeutic dose for the long period of forty-five days. The dogs were never given more than five times the therapeutic dose, nor for a longer period than seventeen days. The effects produced on the liver were evaluated by histological examination of pieces of liver tissue removed from the animals by biopsy, adequate controls being established by the comparison with untreated animals under identical conditions. In all cases in which cinchophen was given, evidence of toxic spoiling of the liver cells was obtained, the degree of damage varying with the amount of the drug ingested. Some of the animals were reexamined after a recovery period, and all but one showed complete repair of the spoiling. The one exception was a dog given a large dose and reexamined one month after the administration of the drug ceased. It is of interest to learn that urobilinogen tests and estimation of the icterus index gave no indication of the degree of liver damage found by microscopical examination.

It is always risky to draw deductions from animal experiments with reference to man, but this work at least shows that the cinchophen drugs are readily capable of producing hepatic spoiling in animals of varying susceptibility. It will be noted that the experimental periods were far longer than those employed by careful clinicians in the treatment of gouty and rheumatic states with these drugs. The authors suggest that the greater resistance of the rabbit is related to the higher proportion of carbohydrate in this animal's diet as compared with that of the dog, and though there is no evidence that this idea is based on fact, it would seem to be sound practice to combine the administration of cinchophen with the prescribing of a diet of high glucose value, in order to spare the glycogen reserve of that organ.

The authors conclude from their study that the therapeutic use of this group of drugs is not justified, in view of their toxic possibilities. This seems rather an extreme view. There does appear to be a place for cinchophen in therapeutics, but it is essential that it should be administered over short periods only. The severe and fatal accidents have practically all occurred when the drug was self-administered, without adequate safeguards, and not under medical advice. It should be impossible for the lay public to obtain this potent preparation except by direct order of a medical practitioner, and all members of the medical profession should be alive to the effects it may have on the liver.

CANCER OF THE CERVIX UTERI IN NULLIPAROUS WOMEN.

THAT lacerations attendant on parturition often precede cancer of the *cervix uteri* is widely recognized. Such emphasis is laid on this sequence of events that the possible occurrence of cancer in the cervix of nulliparous women may be forgotten altogether. It is therefore of practical interest to read a report by Louis E. Phaneuf of three cases occurring in *nulliparae*.¹ Since Phaneuf saw these three patients within the space of five months, he concludes that cancer of the cervix of *nulliparae* is "not uncommon"; the conclusion is scarcely justified, but the report is none the less interesting on this account. The ages of the three patients were twenty-five, twenty-eight and thirty-four years. One was single, one was a widow and one was married. Unfortunately, Phaneuf describes in considerable detail the findings on physical examination, the treatment and the subsequent progress of the patient without discussing the possible ætiological factors. One patient "claimed to have had no serious illnesses in the past", another had a past history which was "unimportant", the third had appendicectomy performed several years previously, but otherwise had always been well. Presumably this may be taken to indicate that Phaneuf is satisfied that none of the three patients had suffered from gonorrhœa or other infective process. Since infection of the cervix by such organisms as the gonococcus is likely to produce an irritative lesion of type commonly held to precede cancer of the cervix, the exclusion of such an infection is most important. Infection must be borne in mind also when prophylaxis is considered. Phaneuf points out that in the campaign against cancer of the cervix it is recommended that all women who have had children be examined twice a year and that all irritative lesions of the cervix be adequately treated. He would go further and subject all nulliparous women to this type of examination. This may be ideal, but is certainly not practicable. If care is taken to eradicate infection and to investigate abnormal symptoms without delay, requirements will be met as far as *nulliparae*, particularly the unmarried, are concerned.

¹ Archives of Internal Medicine, June, 1932.

¹ The New England Journal of Medicine, April 21, 1932.

Abstracts from Current Medical Literature.

THERAPEUTICS.

Treatment of Malaria.

P. MÜHLENS (*Münchener Medizinische Wochenschrift*, April 1, 1932) describes the action of the synthetic drugs "Plasmochin" and "Atebrin" in the treatment of malaria. The latter was used in 122 cases in doses up to 4.8 grammes without ill-effects. When it was administered over a long period, an icteric pigmentation of the skin was noted. This was due to acridin dyes and did not connote any liver damage. The discoloration disappeared within three weeks. The author found it more useful with the schizont than with the gamete forms of malaria. "Plasmochin" acts mainly on the gametes, and a combination of both drugs is ideal. The initial dosage should be 0.1 gramme of each, thrice daily for seven to ten days. In severe cases quinine should be given intramuscularly for the first two days. "Atebrin" is well tolerated by patients unable to take quinine, and is useful for those with black water fever. For prophylactic treatment the author recommends two tablets daily, composed of 0.125 gramme of quinine and 0.01 gramme of "Plasmochin".

Acetyl-Choline Hydrochloride in Peripheral Vascular Disease.

W. C. WATERS (*Annals of Internal Medicine*, April, 1932) reports three cases of trophic lesions due to vascular disease of the extremities treated with acetyl-choline hydrochloride. Acetyl-choline is a powerful dilator of the arteries and arterioles, but not of the capillaries. Ophthalmoscopic examination following its administration reveals dilatation of the central artery of retina to twice its normal size, while there is an absence of flushing of the face. Acetyl-choline should be given intramuscularly or subcutaneously, as taken orally it is without effect, and when given intravenously it is highly toxic. The dosage varies from 50 to 100 milligrammes repeated at twelve or twenty-four hour intervals. As improvement occurs this may be reduced to once, twice or three times a week. Relief has been reported following its use in Raynaud's disease, *thrombo-angiitis obliterans*, and trophic lesions. In evaluating the effectiveness of treatment, the estimation of the cutaneous temperature is of extreme importance. In the cases reported surface temperatures were taken after exposing the extremities to a room temperature of 21.1° C. (70° F.) for thirty minutes. The bulb of a mercury thermometer was then placed between the bases of the first and second toes, which were strapped together. Readings were made after three minutes. In one to three hours after the administration of acetyl-choline the cutaneous temperature

was elevated from 2° to 5° C. The mouth temperature was unaffected. The elevation of temperature lasted from eighteen to twenty-four hours, at the end of which time there was a drop to the original level. Accompanying the reaction were a sense of warmth and a relief of pain in the affected extremities. The administration of the drug daily or every other day over a period of time produced an increase of the surface temperature to a constantly higher level and complete relief of pain. A reduction of the surface temperature after the drug has been discontinued should be accepted as an indication that the drug is still required.

Pneumonia.

R. L. CECIL AND N. PLUMMER (*The Journal of the American Medical Association*, March 5, 1932) record the study of one thousand cases of pneumococcus Type II pneumonia, with especial reference to serum therapy. A combination of the mouse method and of the Krumweide and Sabin methods of typing has enabled laboratory workers to determine the type of pneumococcus in a high percentage of cases of pneumonia in one to five hours. Of 4,310 pneumococcal pneumonias, 32.1% were due to Type I, 23% to Type II, 11% to Type III, 33.8% comprised a large number of infrequent types. In children under twelve, only nine out of 329 cases of pneumonia were due to pneumococcus Type II. Type I and Type II occurred chiefly in persons leading active lives and exposed frequently to contact infections; both these types occurred mainly in January, February and March. Empyema was noted twice as often in Type I pneumonia as in Type II, whereas pneumococcus endocarditis was much more frequent in Type II, in which variety 46.4% of patients had Type II pneumococci in the blood at some stage of the disease. At Bellevue Hospital 48.8% of patients with Type II pneumonia died. This high figure may be due to a high incidence of alcoholism. The death rate was very high in those patients in whom bacteriemia was noted (87.5% of deaths). The death rate was highest in patients over sixty years of age. In treatment since 1924 Felton's concentrated antipneumococcus serum was used in alternate patients with Type II pneumonia. After a preliminary test for sensitiveness to horse serum, five cubic centimetres of concentrated serum were slowly injected intravenously. If no reaction occurred, 10 to 20 cubic centimetres were introduced into the blood stream one or two hours later, and repeated until 40 to 100 cubic centimetres (100,000 to 200,000 units) were given in twenty-four hours. This dose was repeated each twenty-four hours until signs of recovery were noted or until it was evident that the serum was exerting no influence whatever on the disease. The results were not striking, but the impression was that toxic symptoms were lessened. Bacteriemia was diminished by serum

treatment. During 1930-1931 serum treatment was given only to patients admitted to hospital within seventy-two hours of the onset of their infection. The results in 21 cases were very good, only three deaths occurring, compared with 13 deaths in 20 control patients who were not given serum. So far the good results of serum treatment in Type I pneumonia has not been confirmed for Type II, but with the concentrated serum used early in Type II pneumonia improved results may be expected.

Disseminated Sclerosis: Experimental "Vaccine" Treatment.

J. PURVES-STEWART AND F. D. M. HOCKING (*The Lancet*, March 19, 1932) report the results of treatment of a further series of patients suffering from disseminated sclerosis by autogenous "vaccine" prepared from the ultra-microscopic spherula described by Chevassut as occurring in the cerebro-spinal fluid in disseminated sclerosis. Critical examination of Chevassut's work by independent observers has given conflicting results and the authors have dissociated themselves from her. The spherula is not specific to disseminated sclerosis. A similar spherula is found in the cerebro-spinal fluid in other organic nervous diseases and in pus-containing serous fluids from the pleura and peritoneum and from syphilitic chancre. Spherules are not obtained from uncontaminated cultures of the cerebro-spinal fluid from normal persons. In view of the uncertainty as to whether the spherula is a virus or merely a biochemical precipitate, they admit that the accuracy of the term "vaccine" as applied to the preparation used for treatment is open to criticism. One hundred and one patients were treated in the present series. These are classified as early (22), moderate (62), and advanced (17) cases, according to the stage of the malady which had been reached when the patient first came under observation. Repeated courses of autogenous "vaccine" prepared from the spherula cultured in the cerebro-spinal fluid were administered in all cases. In most cases the dose was graduated from one million to two hundred million or more, and the ordinary duration of a "vaccine" course was twelve weeks. Before a fresh course was started careful observations, clinical and serological, were carried out in every case. Among the early cases 14 patients showed definite clinical improvement, and in eight instances the clinical signs and symptoms ceased to advance. One patient of this group, however, after improving clinically for several months, relapsed to his previous state, while another, after improving for a year, had a severe relapse, became steadily worse, and is now in an advanced stage. Among the "moderate" cases 25 patients improved clinically, 26 ceased to advance, and 11 continued to deteriorate. The cases of longest standing were not necessarily the most obstinate. In the advanced cases wide-

spread degenerations and sclerosis were already well marked. Of the 17 such patients, five continued to get worse, while in the remaining 12 the clinical signs and symptoms remained *in statu quo*, three of them finding a definite alleviation of their muscular spasticity.

Cardio-Vascular Syphilis.

H. H. HAZEN (*American Journal of Syphilis*, July, 1932) deals with the treatment of cardio-vascular syphilis, including aneurysm, aortic insufficiency, aortitis, coronary disease, congestive failure and chronic myocarditis in syphilitic subjects. He concludes from his observations that the dangers of treatment of these conditions with arsenical preparations has been exaggerated. He advocates that in all cases in which full anti-syphilitic treatment has not been carried out, a course of iodides or bismuth should be given, and this should be followed by alternating courses of treatment with an arsenical preparation, such as "Novarsenobillon" in small doses, and mercury or bismuth, for twelve months. Treated on these lines, forty patients with aneurysm lived an average time of thirty months from the commencement of observation, as compared with ten patients untreated who lived eleven months on an average. In patients with aortic insufficiency treatment on these lines did not appreciably prolong life in comparison with untreated patients. Two patients with heart block who gave positive Wassermann reactions recovered completely; the myocardial disorders were not appreciably affected. It seems to be generally agreed that arsenical treatment is contraindicated in syphilitic coronary disease.

NEUROLOGY AND PSYCHIATRY.

The Blood Volume of Epileptics.

MORGAN B. HODSKINS, RILEY H. GUTHRIE AND JAMES Z. NAURISON (*American Journal of Psychiatry*, January, 1932) criticize the various modern attempts to control epileptic seizures by starvation, ketogenic diet, dehydration and ingestion of acid-forming salts. They recognize epilepsy as a symptom-complex associated with a variety of superficially unassociated conditions; and they assume that in every epileptic there is a variable cerebro-spinal abnormality which makes the individual more susceptible to seizures, and that vaso-constriction precipitates the attack. They claim that in order to produce a convulsion there must be: (i) a primary variable pathological lesion in the cerebro-spinal system, (ii) an adequate amount of body fluid, and (iii) a vaso-constriction as the precipitating agent. They direct attention to the fact that epilepsy is less frequent in pathological conditions associated with dehydration and low blood volume. In their studies of the blood volume of 78 epileptics and 42 non-epileptic controls, the

results would appear to support the contention of Gamble that there is a disturbance of water metabolism in all epileptics. A trend towards higher blood volume values was found in 78 epileptics, as compared with 42 controls, while low blood volume values were found during convulsive seizures and during fainting attacks. Finally, this investigation gives corroborative proof that the work of Lennox and Cobb, which showed that alkalosis, oedema and decreased oxygen tension were conditions which favoured the onset of epileptic seizures, while in states of acidosis, tissue dehydration and increased oxygen tension epileptic seizures were diminished or absent.

Suprasellar Cholesteatoma.

HERBERT OLIVECRONA (*Brain*, Volume LV, Part 1, 1932) presents two cases of suprasellar cholesteatoma, with details of neurological examination and operative treatment and discusses the diagnosis of this condition in relation to the chiasmal syndrome. The suprasellar cholesteatoma is a congenital slow-growing tumour of the suprasellar region, and therefore likely to cause neurological symptoms at an early age. This helps to distinguish it from meningiomata which occur much later in life. The chief symptoms leading to the diagnosis of this condition are: a slowly progressive primary optic atrophy with bilateral hemianopia occurring in a young person (usually under thirty years of age), an essentially normal *sella turcica*, but with widening of one or both optic foramina and pressure absorption of one or both anterior clinoids and of the *sulcus chiasmatis* of the sphenoid bone, and complete absence of signs of pituitary insufficiency. Suprasellar cholesteatomata yield favourably to operative treatment.

The Gold Sol Reaction in Disseminated Sclerosis.

FOLLOWING a review of the now extensive literature on colloidal reactions in organic diseases, Helen J. Rogers (*Journal of Neurology and Psychopathology*, January, 1932) reports upon a study of the Lange gold sol curve in 70 cases of clinically established disseminated sclerosis. All doubtful cases were excluded from the study, as were those in which at any time a positive reaction to the Wassermann test was obtained either in the blood or cerebro-spinal fluid. In these seventy cases the author found considerable variability, 25% showing the so-called "paretic" curve and the remaining 50% yielding almost every possible intermediary type of curve. It was found that no parallel could be drawn between the type of curve presented and the clinical course followed by the malady, and also that alteration of the gold sol curve occurred spontaneously as frequently as it did after treatment.

Experimental Catatonia.

GEORGE W. HENRY (*American Journal of Psychiatry*, January, 1932) claims to have produced a state of

catatonia in certain mammals by the injection of bulbo-capnine. These reactions were in every way similar to those seen in certain types of *dementia præcox*, and in as much as the phenomena could not be produced in fish, frog or lizard, the author claims that they are dependent upon the degree of development of the nervous system (more particularly the neo-cortex). Bulbo-capnine is an alkaloid resembling apomorphine; and the injections varied in strength from 5% to 10% of the body weight of the animal. Somewhat similar results were obtained by the injection of large doses of *cannabis indica* and mescalin. Such experiments, the author claims, lend weight to toxic factors in the aetiology of human catatonia.

The Tonic Pupil.

W. J. ADIE (*Brain*, Volume LV, Part 1, 1932) describes a non-syphilitic disorder characterized by tonic pupils with or without absent tendon reflexes; and this condition is fully discussed in relation to differential diagnosis from the Argyll Robertson phenomenon and internal ophthalmoplegia. In its most typical form the tonic pupil is usually unilateral and almost always larger than its normal fellow. It is never miotic. Some abnormality of the tendon reflexes most generally accompanies the tonic pupil. Loss of one or both ankle jerks is most frequently found. Asymmetrical reflexes are not uncommon. The family history of patients exhibiting this condition shows no evidence of neuropathic or degenerate stock. The patients are not nervous; nor do they conform to any special physical type. The disorder may be practically symptomless. The complete form of the disorder is characterized by the presence of the tonic convergence reaction in pupils only apparently inactive to light and absence of one or more tendon reflexes. Incomplete forms occur without abnormality of the tendon reflexes. The author believes it to be a benign disorder dependent upon some disorder of the vegetative nervous system. Its importance lies in its being entirely unrelated to neurosyphilis.

The Neurotic Criminal.

PHILIP GETSON (*Journal of Nervous and Mental Diseases*, May, 1932) publishes a psychological study of a neurotic criminal who committed three impulsive burglaries. These acts were the expression of a neurotic need, the solution of an intrapsychic conflict. The author recognizes three types of criminal: the normal individual, who commits a crime under acutely abnormal circumstances; the chronic criminal (neurotic), who in criminal environment develops a criminal *super-ego*; and the criminal of organic degenerative stigmata (the mental defective). He pleads for the recognition and differentiation of these types, so that crime due to illness, whether of body or mind, may be treated instead of being punished.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE SOUTH AUSTRALIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Darling Building, University of Adelaide, on August 25, 1932, Dr. S. J. POOLE, the President, in the chair.

Premedication with Barbiturates.

DR. GILBERT BROWN read a paper entitled: "Premedication with the Barbiturates" (see page 437).

In opening the discussion, DR. ALLAN LAMPHEE said he wished to congratulate Dr. Gilbert Brown upon his most interesting and instructive paper. He mentioned that although he had not used the barbiturates very much, he had been very impressed with the results in the cases in which they had been used. The patient came into the operating theatre so drowsy as not to have the slightest apprehension. The anæsthetic was taken well and there was very little post-anæsthetic vomiting. The effect was much better than that of morphine and hyoscine. Of late years so many different anæsthetics had been introduced that one was sometimes bewildered. Occasionally an anæsthetist was asked by the surgeon to give an anæsthetic which was unsuitable for the operation to be performed. In many cases the patient had made the request, chiefly because he dreaded ether. The fact remained, however, that ether was still the safest and best anæsthetic for the majority of cases, and Dr. Lamphee hoped that, as the result of Dr. Brown's paper, patients would be told that they need not dread an ether anæsthetic any longer.

DR. E. COUPER BLACK congratulated Dr. Gilbert Brown on the interesting paper he had delivered and on having introduced the subject to Adelaide. Dr. Black had had no opportunity of trying the barbiturates intravenously, but had used small to moderate doses of "Sodium amytal" by mouth as a pre-narcotic. The intravenous preparations had been unobtainable in Adelaide. Dr. Brown was fortunate in having some. Dr. Black understood that they were rather expensive, and that might be a factor against their use in private practice unless the fee were worth while. Did Dr. Brown give morphine as a routine? He had heard Dr. Brown say that holding on to the syringe for minute after minute was very tiring, and had read that, in midwifery work, while the obstetrician was waiting to judge the full dose, the patient would throw her arms about when a pain came on, needing a couple of nurses to restrain her. He would also like to know if Dr. Brown thought "Nembutal" showed up better than "Sodium amytal" as regards fatalities or complications. He was very keen on the basal narcosis idea and had used "Avertin" a good deal and found it very satisfactory and safe, especially in children; the only patient who had caused any worry was an adult. He agreed with Dr. Lamphee that the barbiturates toned down the unpleasantness of ether and made the use of the latter easier.

DR. J. CLOSE said that in regard to the patient of his mentioned by Dr. Brown, the main point, in his opinion, was a marked arteriosclerosis, associated with a fairly high blood pressure. On account of this the man was not "a good case" for either anæsthetic or operation, and for several months his renal condition had given Dr. Close some serious thought. A time was chosen for the operation, however, when the renal function was satisfactory, as deduced by dye and urea concentration tests from the good side; the blood urea was also satisfactory.

The day after the operation, when unconsciousness continued, the blood urea was estimated again and was found to be very little, if at all, raised; he was also secreting some urine, five or six ounces being drawn off by catheter on two occasions, but as the patient was sweating very profusely, such an oliguria could be accounted for without blaming the kidney function. The urine was, in addition, very concentrated, of high specific gravity and contained a large percentage of urea. On account of these facts Dr. Close did not regard the man's condition as uræmic.

The suggestion was made that the kidney was exercising a selective action by secreting waste nitrogen and ignoring the "Sodium amytal", or that the sclerotic condition of his cerebral vessels might account for some temporary disturbance of cerebral function.

Dr. Close felt bound to comment on this case, as Dr. Brown, no doubt for the sake of an argument, had challenged him, since from silence it might be inferred that he disapproved of premedication with barbiturates, or that he (Dr. Close) had been trying to shift responsibility. Regarding the first possible inference one had only to see Dr. Brown at work, which opportunity Dr. Close frequently had at the Adelaide Hospital, to realize the care and efficiency of the anæsthetist, as well as the good results attained.

Dr. Gilbert Brown thanked the members. He explained the breath-holding test, which he considered as the most useful single test in determining the fitness of a patient for general anæsthesia. The patient sat perfectly quiet for five minutes, then drew a full, but not abnormally deep, inspiration. The breath was then held with the mouth closed and the nostrils compressed with the fingers, while the time was noted. The normal period for which the breath could be held in this manner was thirty to forty seconds. The variations from the normal were classed: (i) Under two seconds, unfit for any general anæsthetic; (ii) ten to eighteen seconds, "poor risks"—some might be fit for a short gas and oxygen anæsthetic; (iii) eighteen to thirty seconds, subnormal, but probably "fair risks"; (iv) over thirty seconds, probably "good risks". This test alone, of course, could not be considered enough without a general examination.

In reply to Dr. Lamphee, Dr. Gilbert Brown agreed that sometimes a request was made for a gas anæsthetic when it was not absolutely essential and that a more suitable one might be either preceded by a barbiturate. But there were occasions when the gas anæsthetics were specially indicated in major abdominal surgery in patients who were suffering from other diseases. In such patients it was possible to give better relaxation when the barbiturates were included in the premedication.

In reply to Dr. Couper Black, morphine had been used in some cases, but purposely omitted in others. The percentages had been worked out as to complications and deaths for the different barbiturates used, but the numbers were too small for them to be of any value as statistics. There were certain difficulties with the intravenous method. Sometimes it was difficult to insert the needle into a vein. It was also easy to put the needle through the vein or displace it when it was necessary to hold both needle and syringe still for ten minutes and press the piston every fifteen seconds, which meant forty injections. The oral method was quite satisfactory for most cases, although the dosage could not be gauged with the same precision.

Dr. Close had risen to the bait and had joined in the discussion, as Dr. Brown had hoped. Undoubtedly the dose of "Sodium amytal" had been too large considering the poor renal function in Dr. Close's patient. But there was a certain amount of uræmia present, and the absence of corneal reflex was not noticed in any other patient. Dr. Bollen had inquired whether Dr. Gilbert Brown would give a barbiturate before an anæsthetic to himself. The answer was "yes", and that once, when the supply of "Nembutal" was low, Dr. Gilbert Brown had kept back four capsules in case he required an anæsthetic himself before the end of the three months required to obtain further supplies from America.

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Melbourne Hospital on May 13, 1932. The meeting took the form of a series of clinical demonstrations by the members of the honorary staff.

Tuberculous Disease of the Kidney.

DR. BASIL KILVINGTON showed two patients who were suffering from tuberculous disease of the kidney. In each instance the kidney had been removed and multiple

stones, producing destruction of the organ with pyonephrosis, had been found.

The first patient was a man, aged fifty-three years. His urine had contained albumin and pus, and *Bacillus coli communis* infection was discovered. On cystoscopic examination a cystitis was found; from the right ureter pus due to *Bacillus coli communis* infection was recovered; no pus was present in the urine from the left ureter, but some streptococci were found. X ray examination revealed a right renal calculus, and a pyelogram showed that a right hydronephrosis was present. When the dye test was carried out, the dye appeared from the left ureteric orifice in seven minutes, but no dye appeared from the right orifice in fifteen minutes. In this case nephrectomy was complicated by dense adhesions around the kidney.

The second patient was a man, aged twenty-eight years; his tuberculous disease involved the kidney, ureter, bladder and prostate. On cystoscopic examination, the right ureteric orifice was seen to be surrounded by tuberculous ulceration, the left orifice was clear. When the dye test was performed, dye appeared at the left ureteric orifice in five minutes, but none appeared at the right orifice in fifteen minutes. When the right kidney was removed, it was found to be large, some perinephritis was present at the lower pole, tuberculous areas were seen on the surface of the kidney, and the ureter was very thick and tuberculous. During convalescence the wounds became infected with tuberculosis.

Fracture of the Femur.

Dr. Kilvington also showed four patients who were suffering from fracture of the neck of the femur. They had been treated by a fibular graft and by placing the leg in plaster, as described by Whitman. Dr. Kilvington said that this method gave a better result than any mode of treatment. The bone graft made this more certain than a pure plaster immobilization (Whitman) and was essential where the fracture was of three or more weeks' duration, for after this interval union did not seem to take place by any method of fixation. It could be used in all but the very old and bronchitic subjects, and there was little shock, for the joint itself was not exposed. The time taken in this procedure was a factor, for the whole process, including application of plaster, took from one and a half to two hours.

The following were briefly the steps taken. The patient was anaesthetized with nitrous oxide and oxygen, for this gave all the relaxation necessary. He was placed on an Ord's fracture apparatus and extension was made till all shortening was relieved, but with care not to produce over-extension. The leg and foot were rotated from 12° to 15°. The leg was fully abducted at the hip. An incision from 15 to 20 centimetres (six to eight inches) was made lateral to the trochanter to expose the femur. The drill was entered one centimetre below the ridge on the trochanter and was directly horizontal to the opposite anterior superior iliac spine. It was two centimetres in diameter and should penetrate the bone for a distance of not more than ten centimetres (four inches). Otherwise, it might penetrate the articular surface of the head into the joint. When the surgeon was unaccustomed to this operation it was well to have an X ray examination made while the patient was under the anaesthetic to see that the drill had not missed the neck and head. The required length of fibula was removed and was then hammered into the drill hole, the excess of length being cut off flush with the trochanter. The wounds were sewn up with catgut and the limb, including the foot and pelvis, put up in plaster with the knee slightly flexed.

Dr. Kilvington's rule was to leave this on for three months. The next three months were spent in bed, but with massage, and the patient was encouraged to perform all limb movements, but no weight was borne on the leg. For the next three months he was allowed to walk, but part of the weight was taken by a Thomas knee splint with calipers in the heel. After nine months he was encouraged to walk without any mechanical assistance. The results were in most cases excellent and in many

almost perfect, but full recovery could not be expected under twelve months.

Myeloid Sarcoma of the Tibia.

Dr. VICTOR HURLEY showed a male patient, aged twenty-seven years, who was first seen in May, 1931, with a history of having strained his right knee while getting down from an office stool nine months previously. Three months after the injury the patient complained of pain about the inner side of the knee, located over the head of the tibia. The pain persisted and sometimes the patient had "starting pains" at night. On X ray examination the characteristic appearances of myeloid sarcoma of the head of the tibia were seen. At operation the vascular tumour of the head of the tibia was removed by curettage and chiselling. The cavity was carbolized and packed. Subsequent deep X ray therapy was used, four applications being given. Local recurrence of the growth took place with extension down the shaft of the tibia and into the soft tissues. After consultation, amputation above the knee was advised and was carried out before the date of the meeting. Pathological examination revealed a giant cell sarcoma.

Dr. Hurley said that this case illustrated the possible relationship between injury and sarcoma and it also demonstrated the points in the treatment of myeloid sarcoma. Some tumours of this kind were cured by local removal. In others, local recurrence or metastases sometimes occurred. The perforation of the bone cortex discovered on the first X ray examination was evidence of the infiltrating character of the growth and it was a point for discussion whether such a growth was malignant from the onset or whether, originally benign, it developed malignant characteristics.

Appendicitis in a Patient with a Permanent Gastrostomy Opening.

Dr. Hurley also showed a woman, aged twenty-five years, who suffered from acute appendicitis. The case was interesting because a gastrostomy opening had been present for eleven years and during this time the patient's general condition was well maintained. The gastrostomy was done on account of a complete stricture of the oesophagus due to swallowing caustic soda at the age of fourteen years. The patient's appendiceal symptoms were characteristic. Nausea was present, but, of course, vomiting was not possible. When food was given by the gastrostomy tube, however, the patient felt a desire to expel it immediately. The tongue was coated and the breath was typically "abdominal". Post-operative progress was uneventful.

Stone in Common Bile Duct After Cholecystectomy.

Dr. Hurley's third patient was a woman, aged forty-nine years, who had a typical history of recurrent attacks of cholecystitis, and at operation a year ago a large, thick-walled gall-bladder, packed with numerous small stones (one hundred or more) was removed. The common bile duct was palpated and no stone was detected. Convalescence was uneventful, but within the last three or four months she had suffered from attacks of biliary colic every six weeks. There was no jaundice with these attacks, nor was there in the attacks before her operation.

At the second operation, on May 6, 1932, the head of the pancreas was found to be thickened, and after much searching a small stone, the size of a large pea, was located in the ampulla. This was removed with common duct forceps through an incision in the supraduodenal part of the duct. Probes or catheters could not be passed through into the duodenum, but fluid injected along a catheter in the duct ran freely into the duodenum. The common bile duct was drained with two catheters, and through the lower catheter fluid was syringed into the duodenum each day.

In another patient, operated on the previous month, the gall-bladder had been removed nine years previously in England. Attacks of biliary colic began four years after operation and persisted. There was no jaundice in this case either. At operation several stones and much biliary mud were removed from the common bile duct.

Dr. Hurley pointed out that in both cases stones were removed from the common bile duct after a previous cholecystectomy. In neither case was jaundice present with the attacks. The question arose as to how long the stones had been present in the duct. Were they overlooked at the first operation, or did they find their way into the duct subsequently from the liver?

Megacolon with Volvulus.

Dr. Hurley also showed a man, aged forty-nine years. Ten years before the patient was admitted to the Melbourne Hospital with intestinal obstruction, large bowel in type, and of some days' duration. At operation a volvulus of the sigmoid colon was found, with two largely distended loops of bowel, possessing a narrow base of attachment to the posterior abdominal wall. The affected bowel was resected and a side-to-side anastomosis was carried out after closure of the resected ends. Three days later caecostomy was done because of intestinal distension. Subsequent operations were necessary to close the caecostomy and a faecal fistula which persisted at the site of the anastomosis. The patient eventually made a good recovery and remained well until a month before, when he suffered from chronic intestinal obstruction, vomiting, and marked abdominal distension. There had not been any bowel action for four days, despite enemata *et cetera*.

He was admitted to hospital and X ray films taken after a barium enema revealed an enormous distension of the colon; visible coils of bowel were present. At operation a similar condition of distension of the transverse colon was found as had been present in the sigmoid ten years previously. While no definite volvulus existed, there was considerable tension and some rotation of the attachment of the transverse mesocolon. Resection of the transverse colon, splenic flexure and part of the descending colon was carried out and a caecostomy performed. Convalescence was smooth and normal and daily bowel action now occurred without any difficulty. The patient was taking one ounce of paraffin oil daily.

Dr. Hurley said that this case was of interest in that the condition of megacolon and volvulus of the sigmoid which was present in the first instance, again manifested itself ten years later in the remaining part of the colon. Between the two operations the patient was perfectly well and did not lose any time from his work.

Hydatid of the Kidney.

Dr. Hurley also showed a man, aged fifty-two years, who had had symptoms of hydatid disease of the left kidney, commencing probably from the age of eighteen years. Every few months he had suffered from an attack of left renal colic and passed pus and "grape skins" in the urine.

In 1924, Dr. Derham detected laminated membrane, scolices and hooklets in his urine, and about the same time he had anginal symptoms with cyanosis. His cardiac condition improved under treatment, and in November, 1931, he was seen by Dr. Silberberg, who reported a fair cardiac efficiency and a normal electrocardiographic tracing. Eight years before he was seen in consultation by another physician, who thought his general condition made operation undesirable.

His renal attacks had, however, persisted, and were becoming more severe and frequent. His left kidney was not palpable, but tenderness was present over it on deep percussion.

On April 19, 1932, investigations were carried out to determine the condition of his urinary tract. On cystoscopic examination the bladder was normal, both ureteric orifices were clearly seen, the left opening was drawn slightly upwards and to the left, and this orifice was larger and rounder than the right. Five cubic centimetres of indigo-carmin were injected intravenously and appeared from the right ureter in three to four minutes. The left ureter was catheterized and eighteen cubic centimetres of a 15% solution of sodium iodide introduced. Dye escaped from this catheter in fifteen minutes. A pyelogram of the left kidney was then obtained. These films showed a large rounded cyst communicating with the upper pole of the left kidney. The casein reaction was markedly

positive. He had reaction following this examination, with rise of temperature, pain, tenderness, and rigidity over the left kidney, and increased pyuria. This had since settled down and he was now awaiting operation.¹

Thrombosis of Cerebellar Artery.

DR. IVAN MAXWELL showed a male patient, aged fifty-five years. The evening before admission to hospital he complained of vertigo, nausea and vomiting. He retired early to bed and on attempting to rise next morning found that he lurched violently to the right, so much so that it was impossible for him to stand. He was admitted to hospital on February 10, 1932, and was then unable even to sit up in bed unsupported. Physical examination revealed slight loss of power in the right arm and nystagmus on looking to the right. There was intention tremor and dysidiadochokinesia of the right arm and pass-pointing to the right. Posterior column conduction of both sides was normal. The plantar reflexes were flexor. Sensations of pain, heat and cold were not appreciated on the left leg, left half of the body and left arm, but were normal on the left half of the face and the whole of the right side. The cerebro-spinal fluid was microscopically normal and there was no increase in globulin. The Wassermann test applied to blood and cerebro-spinal fluid gave no reaction. The colloidal gold reaction was normal. The blood urea was 36 milligrammes per 100 cubic centimetres. The patient's hearing was diminished in both ears. Investigation of the function of the semi-circular canals by caloric tests was unsatisfactory. The fundi were normal, but a traumatic cataract was present in the right eye. His blood pressure was systolic 130, diastolic 90 millimetres of mercury. The patient's condition was diagnosed as thrombosis of the right posterior inferior cerebellar artery, and he was treated with potassium iodide and intravenous injections of 15% sodium chloride, one hundred cubic centimetres being given at each injection. His condition gradually improved and he was later sent for reeducational exercises in the physiotherapy department. He had made so much progress at the time of the meeting that he could walk moderately well with the aid of a walking stick.

Multiple Calculi in a Movable Kidney.

Dr. Maxwell's second patient was a female, aged fifty-five years, who first noticed a large lump in the right lumbar region of the abdomen some twelve months previously. It was not painful and had not increased in size during the period since it was first observed. Physical examination revealed an oval, firm, smooth swelling situated in the right lumbar region, movable on respiration and having limited mobility on palpation. Pelvic examination indicated that it was neither uterine nor ovarian in origin. A barium enema revealed no abnormality of the bowel, and failure of response to the Casoni and complement fixation tests excluded a hydatid cyst. X ray plates of the right renal area showed an abnormally placed and enlarged right kidney containing multiple calculi. The indigo-carmin test indicated normal function of the left kidney, but no dye appeared from the right ureter even after twenty minutes. The urea concentration test gave figures of 1.6% and 1.9% in the first and second hours. The urine contained no pus cells, red corpuscles or crystals, but on incubation yielded *Staphylococcus albus*. In view of the possible future infection of the right kidney containing the calculi, Dr. Searby advised nephrectomy, but the patient was loath to have any operative procedure so long as she remained free from symptoms. A diet low in oxalate-containing foods or in nucleo-protein was prescribed and sufficient citrate to prevent the urine becoming acid was given.

Auricular Fibrillation.

Dr. Maxwell's third patient, a male, aged fifty-eight years, had been under treatment for auricular fibrillation since 1928. He was presented as an illustration of remarkable cardiac compensation, for, despite the fact that his apex

¹ A few days after the meeting the hydatid cyst, with many daughter cysts, was removed by operation, the kidney being left *in situ*. The patient made an uneventful recovery.

beat was 17.5 centimetres (seven inches) from the mid-line and in the sixth intercostal space and was associated with gross aortic and mitral regurgitation, the patient continued practically free from all signs of oedema over a period of four years till within a few days of the meeting, when passive congestion of the liver and oedema of the legs appeared. The Wassermann test yielded no reaction and his blood pressure was within the normal limits. In the latter months the amount of tincture of digitalis necessary to maintain the pulse rate between 70 and 80 was only 1.0 mil (fifteen minims) per day. In his case it was not thought desirable to attempt to restore normal rhythm by the administration of quinidine.

Aneurysm of the Subclavian Artery.

Dr. Maxwell's fourth patient, a female, aged fifty-two years, had noticed a pulsating swelling in the right side of the neck for several months. It was not accompanied by pain or headache, but she experienced dyspnoea during exertion. On examination the pulsating tumour was found to be situated just above the *manubrium sterni* and the inner end of the right clavicle. The apex beat was in the fifth space, 11.5 centimetres (four and a half inches) from the mid-line. A systolic thrill was present over the tumour. Systolic and diastolic bruits were found both in the aortic and mitral areas of the heart. The blood pressure in the left arm was 150 millimetres of mercury systolic, 86 millimetres diastolic; in the right arm the figures were 180 systolic, 76 diastolic. X ray examination of the chest showed that the heart was slightly enlarged to the left, the posterior mediastinum was clear, the aortic arch shadow was definitely widened, but the pulsatile swelling in the neck was not visible with the screen. The Wassermann test gave a strongly positive reaction. The swelling was regarded as an aneurysm of the innominate artery or possibly the right subclavian artery. Anti-syphilitic treatment with iodides and mercury had been commenced, and it was proposed to administer small doses of "Novarsenobillon" at a later date.

Traumatic Aneurysm of Subclavian Artery.

Dr. A. E. COATES showed a case of traumatic aneurysm of the right subclavian artery treated by ligation of the innominate and common carotid arteries.

A male, aged fifty-one years, was injured by a motor truck in 1927. The right clavicle was fractured and numerous other injuries were sustained. For fourteen months after the accident he could not move the right arm, also he noticed a small lump in the right supra-clavicular fossa. On admission to the Melbourne Hospital in January, 1932, there was a large pulsating swelling above the right clavicle, extending back into the scapular regions. The right radial pulse was weaker than the left. The blood pressure was lower. The trachea was displaced to the left and the right upper limb was useless. Intense pain which prevented sleep was complained of in the forearm and hand. A malunited fracture of the middle of the clavicle was evident. A diagnosis of aneurysm of the right subclavian artery was made. The Wassermann test gave no reaction.

On January 18, 1932, under general anaesthesia, Dr. Coates ligated the innominate artery in two places. The proximal ligation did not completely occlude the vessel and the distal one completely closed the lumen, but did not rupture the middle or inner coats. The common carotid artery was also tied in continuity before the innominate was ligated. Number 5 silk, double, was used for each ligation. Immediate cessation of pulsation in the aneurysm occurred when the innominate artery was occluded. A small piece of the head of the clavicle and of the *manubrium sterni* had to be removed to render the innominate artery accessible. The right upper limb was then wrapped in cotton wool. The radial pulse appeared one week later, and steady improvement in the power of the limb had occurred since. Dr. Coates pointed out that the patient could do all kinds of work and there was a complete absence of pain. The clotted aneurysm had slowly diminished in size and there was no evidence of its presence.

Syphilis of the Ulna.

Dr. Coates also showed a boy of eighteen years who, in November, 1931, was struck by a piece of rubber on the forearm at work. Twenty-four hours after the accident there was over the left ulna a lump which persisted.

In January, 1932, examination showed a spindle-shaped bony swelling arising from the lower ulna. An X ray examination on January 18 revealed "marked irregular periosteal proliferation involving over five inches of shaft of the ulna, no apparent destruction of the cortex". It was stated that if syphilis were excluded, the condition was sarcomatous, possibly of Ewing's type. As the case had a medico-legal interest, biopsy was done on January 27 and the pathological section report was: "section suggests *osteitis fibrosa*, early stage". The Wassermann reaction was "strongly positive" on two occasions.

Intense treatment with "Novarsenobillon", mercury, bismuth and iodine was instituted. On February 11 an X ray examination revealed some increase in the amount of periosteal proliferation on the medial side of the ulna in its distal two inches. Over the lateral side there was less definition about the cortical portion of the ulna, possibly accounted for by some difference in density of films.

On March 10 he was discharged to the out-patient department, on anti-syphilitic treatment, the lump being about the same size. Soon afterwards he returned to work. At the time of showing, the lump on the ulna had entirely disappeared.

Raynaud's Disease.

Dr. Coates showed a patient suffering from Raynaud's disease involving all the fingers of both hands. For seven years the patient, a female, aged forty years, had been unable to do much with her hands on account of pain and coldness.

The fingers were blue and cold, occasionally pale. The terminal phalanges were shrunken and the nails atrophied. The pulp of the fingers was pitted and withered. Periarthral stripping of the brachial artery under local anaesthesia, nine months before the meeting was followed by complete relief of all symptoms. The patient could freely use the hands, which were warm and free from pain. The atrophied condition of the finger pulp and phalanges of course persisted.

Colles Fracture.

Dr. Coates showed a patient with a Colles fracture to illustrate the use of a plaster sandwich which could be moulded to the shape of the forearm and yet permitted accommodation to swelling of the wrist. The flexed position of the wrist was useful. The necessity of using violence in reducing impacted Colles fractures was stressed. In patients seen after several days from the date of injury, much force was required to force the lower fragment forwards. The lateral position radiogram was valuable, indicating the line of the lower articular surface of the radius. This surface should look downwards and slightly ventrally. Unless this articular surface was correct, residual arthritis and weakness in the hand would result, despite the fact that clinically it appeared perfect.

Traumatic Amputation of Both Thighs.

Dr. Coates showed a patient who had suffered traumatic amputation (by railway train) of both thighs in the middle third. The patient, a boy of eighteen, was run over by a train and lay for five hours during a cold night exposed beside the line. He was very shocked when admitted to hospital at 4 a.m. On trimming up the stumps, gaseous crepitus was noted in the muscles cut across. A smear taken revealed *Bacillus welchii*. Injections of gas antiserum were given into the muscles above the stumps, and the raw ends of the thighs were irrigated with dilute hydrogen peroxide. A blood transfusion was also given.

Sloughing of the gangrenous ends of the stumps occurred, but the patient eventually recovered and the ends of the stumps completely covered with skin.

Dr. Coates said that the case was of interest in that the patient was in a very shocked condition and yet resisted a virulent, rapidly spreading gas infection. The gas antiserum seemed to deserve some credit for the patient's recovery.

Thyreotoxicosis.

Dr. F. BLOIS LAWTON showed a woman, aged sixty-nine years, who had been admitted to hospital on May 3, 1932. She had had a "nervous breakdown" three and a half years previously, but from that time had been fairly well until three weeks before admission to hospital, when she had a sudden attack of palpitation followed by dyspnoea, even when sitting still. For three weeks there had been swelling of all limbs and of the abdomen, with pitting on pressure. Her sleep had been disturbed by palpitation. There had been anorexia for one week, and the bowels had been loose for a few days. The patient had been passing very little urine. At the time of admission to hospital there was marked dyspnoea, and the appearance of the face suggested that the patient had lost weight. There was slight cyanosis of the lips, the pulse rate was 114, the temperature 37.2° (99° F.) and the respiration rate 28. The pulse was irregular from extrasystoles, and there was some sclerosis of the radial arteries. The systolic blood pressure was 156 millimetres of mercury, and the diastolic pressure was 52 millimetres. The apex beat was in the sixth intercostal space, 12.5 millimetres (five inches) from the mid-sternal line. There was a soft systolic bruit, and a reduplication of the first sound and numerous extrasystoles were present. There was gross oedema extending from the feet to the clavicles and involving both upper limbs. There was dullness over the bases of both lungs, with some crepitations. The liver margin was palpable two finger breadths below the right costal margin, and there was tenderness over it on pressure. A light diet and restricted fluids were prescribed. Tincture of digitalis, 1.2 mils (twenty minims), and ammonium chloride, 1.8 grammes (thirty grains), were given three times a day.

When the patient was seen on May 6, an emaciated appearance of the face and the high pulse pressure were observed. The thyroid gland was found to be enlarged, firmer than normal, and to contain several nodules, the largest being in the right lobe and in the isthmus. Very little urine was being passed. The amount measured was eight to nine ounces daily, but there was some diarrhoea and some urine was passed when the bowels acted. The patient complained of thirst, and although the oedema had not decreased, the intake of fluids was no longer restricted. She was also given a more liberal diet. Three injections each of one cubic centimetre of "Salyrgan" were given. The patient passed fifty-four ounces of urine after the first injection, seventy-two ounces after the second, and ninety ounces after the third. At the time of the meeting the oedema had decreased and the general condition of the patient had improved. She had not yet been given any iodine. The basal metabolic rate was estimated and found to be + 44%, but on account of her condition this result was not regarded as reliable. The specific gravity of the urine was 1.015; the urine was acid, contained a trace of albumin, but no sugar. Odd hyaline and granular casts were seen. Further inquiries indicated that the nervous breakdown three and a half years previously was almost certainly due to a thyreotoxicosis.

Spontaneous Pneumothorax.

Dr. Lawton also showed a man, aged twenty-one years, who had been admitted to hospital on May 15, 1932. For five years previously he had had a cough with some sputum intermittently, and two years before he had had a pain low down on the right side of his chest. The pain was stabbing in character and was present for twenty-four hours. It made him hunch his shoulders, and he had some difficulty in getting his breath. Six months after this first attack, he had an attack of similar pain on the left side of the chest, and three weeks before admission to hospital there had been another attack of stabbing pain on the right side of the chest. He had no further symptoms and was able to go about actively until the day before he had been seen at the hospital. That day, while walking in the street after lunch, he was suddenly overcome by pain in the lower part of the left side of the chest. The pain was of a stabbing character and made him stop and hunch his shoulders; he had great difficulty in getting his breath. When the patient was admitted to hospital the pain had worn off and he was much easier. In

every attack of pain there had been a cold shiver and a sweat soon after the onset. There was a slight cough, but no sputum since the onset of the present illness. About one year previously the patient had lost about 3.6 kilograms (eight pounds) in weight, and during the last year he had regained 1.8 kilograms (four pounds). There was nothing else of note in the history. On admission to hospital, the temperature was 36.9° C. (98.4° F.), the pulse rate was 88, and the respirations 26 per minute. The patient was not distressed. His chest showed the typical signs of a left-sided pneumothorax, but there were no signs of an effusion. Since admission to hospital the patient had usually an evening temperature of 37.25° C. (99° F.). He was comfortable and no special treatment for the pneumothorax was indicated. The condition appeared to have a tuberculous origin, but before deciding on the form of treatment it was proposed to make further investigations.

Dr. L. E. HURLEY showed a male patient, aged fifty-six years, who first attended the out-patient department on April 28, 1932. The past history included influenza, gonorrhoea and an operation for double inguinal hernia. He had been quite well until February, 1932, when he had a sudden attack of severe pain near the right nipple going through to the scapular region. Deep breathing and coughing had no effect on the pain. Ever since he had noticed considerable shortness of breath, more marked on exertion, but also present to some extent while he was at rest. Moderate exertion also caused a recurrence of the pain in the chest, which was relieved by rest. He had had a dry cough ever since the onset of the pain. His appetite had been good, and he had lost no weight.

Physical examination except for the chest condition revealed no abnormality. Over the whole of the right side of the chest, except in the hilus region posteriorly, the percussion note was slightly hyper-resonant and the breath sounds were much diminished. Near the base of the right lung posteriorly there was distant bronchial breathing. There was no heart displacement, and on inspection both sides of the chest moved equally and well. On the right side there was slight extension downwards of the lower border of pulmonary resonance. The Wassermann test applied to the blood gave no reaction. X ray examination revealed a clear left lung with pneumothorax of the right side and partial collapse of the whole lung.

Dr. Hurley said that the points of interest were:

1. The absence of some of the classical signs of pneumothorax, namely, displacement of organs, the coin sound diminished movement of the affected side, and marked hyper-resonance on percussion.
2. The importance of marked diminution of breath sounds in the presence of a normal or slightly hyper-resonant percussion note in the diagnosis of pneumothorax.
3. The aetiology. The usual cause of spontaneous pneumothorax was the rupture of a small superficial focus of tuberculosis. If the focus were not highly infected a hydropneumothorax usually resulted, but if the focus were large with definite secondary infection, then a pyopneumothorax was usually produced. Simple pneumothorax unaccompanied by fluid might be due to the rupture of an adhesion of tuberculous origin, to the rupture of a cicatricial bulla, the result of a previous minute focus of tuberculosis, or to the rupture of an emphysematous bleb. In rare cases spontaneous pneumothorax was recurrent, as in one patient who had three attacks. In this instance X ray examination of the chest after absorption of the air in each attack showed no abnormality of the lungs. The prognosis in spontaneous simple pneumothorax, when it occurred suddenly without any previous history suggesting disease of the lungs, was good. The occurrence of pneumothorax in cases of known pulmonary tuberculosis was usually poor.

Complete Heart Block.

Dr. Hurley also showed a female patient, aged twenty-one years, who attended hospital first on June 26, 1931. Her mother and father had both died of pulmonary tuberculosis. There had been no previous illnesses, and there was no history of chorea, growing pains or rheumatic fever. For the past eighteen months she had had a cough with a

small amount of yellowish sputum. In the last three months she had lost over a stone in weight. She had also noticed that she tired easily and became short of breath on slight exertion.

On examination the pulse rate was 44 to the minute, and did not vary more than two or three beats with exertion. During her stay in hospital over a period of seven weeks the pulse rate varied between 38 and 56, and on one occasion was 88. A pulse rate of about 80 was also observed in the out-patient department on two occasions. Pulsation of the veins in the neck could be seen, the rate being about 120 per minute. The cardiac apex was in the sixth intercostal space 11.5 centimetres (four and a half inches) from the mid-line. Weak sounds, probably due to auricular contraction, could sometimes be heard. There was a soft systolic murmur at the cardiac apex. At times numerous extrasystoles were present. The Wassermann test applied to the blood gave no reaction on two separate examinations. Electrocardiograms taken on July 2, 1931, and on July 27, 1931, showed the typical appearances seen in complete heart block. X ray examination of the lungs revealed no abnormality, and no tubercle bacilli could be detected in the sputum. Administration of atropine sulphate in doses of 0.6 milligramme (one-hundredth of a grain) three times a day had no effect on the heart block.

Dr. Hurley enumerated the following points of interest:

1. The patient's age. Most cases of complete heart block occurred later in life, and were due to atheroma or arteriosclerosis. Syphilis was the cause in a few cases. Rheumatic infection might also be the cause, and was thought to be the cause in this case, despite the fact that there was no history of rheumatic infection.
2. The occasional reestablishment of normal rhythm.
3. The fact that auricular beats could sometimes be heard.
4. The onset with cough and sputum and marked loss of weight in a patient both of whose parents had died of pulmonary tuberculosis naturally suggested the possibility of a pulmonary lesion, but none could be demonstrated.

Aneurysm of the Aorta.

Dr. Hurley showed two patients with aneurysm of the aorta.

The first was a woman, aged fifty-five years, who came to the out-patient department on August 29, 1931. She had complained of shortness of breath on exertion for the past six years, but much worse in the last few months. She had also had attacks of dyspnoea at night, when she had to sit up to get her breath, and had a good deal of wheezing in the chest. There had also been dull gnawing pain about the left scapular region, and pain in the precordial region made worse by exertion and relieved by rest.

On examination there was marked dullness across the *manubrium sterni* to the extent of about 7.5 centimetres (three inches). Marked pulsation could be seen in the suprasternal notch, and on pressing behind the sternum a pulsatile tumour could be felt. The cardiac apex was in the sixth intercostal space 13.75 centimetres (five and a half inches) from the mid-line. There was one finger breadth of right heart dullness. The systolic blood pressure was 220 and the diastolic 40 millimetres of mercury. A tracheal tug could be felt. X ray examination showed the heart shadow to be much enlarged downwards and to the left. The aortic shadow was much widened, being about twice the normal width. The X ray appearances were thought to be due to an aneurysm, but possibly to a general dilatation of the aorta. The blood gave a strongly positive reaction to the Wassermann test. Iodides and mercury had been given, followed by a course of seven injections of arsenobenzol, the initial dose being 0.1 gramme.

On May 11, 1932, the patient stated that she felt considerably improved, the shortness of breath was much better, the pain in the chest much easier, and not so readily induced by exertion, and she had not had any attacks of nocturnal dyspnoea for some months.

The diagnosis of aneurysm from aortitis with dilatation of the aorta was discussed, and the amelioration of the symptoms following antisyphilitic treatment.

The second patient was a man aged 47 years, who came to the out-patient department on February 15, 1930. His

only complaint had been that for the past two years he had noticed a pain just below the xiphoid process, worse in the morning and at night time, present almost every day, the longest period of freedom being a few days. Even strenuous work had no effect on the pain.

On examination there was a definite area of pulsation over the *manubrium sterni* with about 7.5 centimetres (three inches) of dullness across the sternum. Systolic and diastolic murmurs could be heard at the aortic region. Systolic blood pressure in the right arm was 155, and in the left 125 millimetres of mercury. The left pulse was weaker than the right. A tracheal tug was present. X ray examination showed the heart to be normal in size, the aortic arch widened upwards posteriorly and to the left, and an aneurysm of the aortic arch with the trachea pushed to the left. Electrocardiograms showed inversion of the T wave in lead III, and P wave downward in leads II and III and isoelectric in lead I.

Dr. Hurley said that the patient had had treatment with iodide and mercury and one course of arsenobenzol, seven injections beginning with 0.1 gramme. He felt better and the pain had been completely relieved. The points of interest in the case were: (i) The comparative absence of any severe or typical symptoms of aneurysm; (ii) the relief of the pain by antisyphilitic treatment.

The inversion of the T wave in lead III and the downward P wave in leads II and III were discussed.

Diabetes Mellitus.

DR. W. W. S. JOHNSTON, DR. T. A. F. HEALE and DR. LUCY BRYCE showed two diabetic patients who had been treated with high carbohydrate-low fat diets.

The first patient was a male, aged thirty-six years, who was admitted to the diabetic clinic in July, 1930. The usual diabetic symptoms had been present for twelve months. The urine contained a large amount of sugar and a trace of diacetic acid. The fasting blood sugar was 0.19 per centum. The patient was admitted to hospital and stabilized on a diet of carbohydrate 75, protein 67, fat 150 grammes, representing 1,918 calories, with 12 units of insulin daily. The fasting blood sugar was 0.11 per centum.

After discharge from hospital the diet was gradually raised to carbohydrate 100, protein 77, fat 160 grammes, representing 2,148 calories, with 16 units of insulin daily. Progress during the next six months was not satisfactory. The fasting blood sugar ranged from 0.15 to 0.17 per centum.

In May, 1931, the patient was switched to a diet of carbohydrate 245, protein 95, fat 92 grammes, representing 2,188 calories. Glycosuria was present for three days and was abolished with 24 units of insulin daily. Two weeks later, on the same diet and insulin, the urine was sugar-free throughout the day and the fasting blood sugar was 0.11 per centum.

At the time of the meeting, after one year on the same high carbohydrate-low fat diet, the patient was very well, the urine was sugar-free throughout the day with 12 units of insulin daily. The fasting blood sugar was 0.11 per centum.

The second patient was a male, aged sixteen and a half years, who was admitted to the diabetic clinic in December, 1931. The usual diabetic symptoms had been present for two months. The urine contained a large amount of sugar and a trace of diacetic acid. The fasting blood sugar was 0.26 per centum.

He was admitted to the hospital and stabilized on a diet of carbohydrate 225, protein 80, fat 90 grammes, representing 2,030 calories, with 57 units of insulin daily. The fasting blood sugar was 0.10 per centum.

At the time of the meeting, after six months on the same high carbohydrate-low fat diet, the patient was well, his urine was sugar free throughout the day with 30 units of insulin daily. The fasting blood sugar was 0.12 per centum.

It was explained by Dr. Johnston, Dr. Heale and Dr. Bryce that there was a general tendency to increase the amount of carbohydrate and lower the amount of fat in the diet, which depended on a belief that in the long run

diabetic patients could be made to gain in tolerance, and that they did better when they were utilizing this amount of carbohydrate rather than the old time small amounts.

In the diabetic clinic at the present time they usually prescribed about 150 grammes of carbohydrate, with sufficient protein and fat to make up a maintenance diet. Hardly ever did they give less than 100 grammes of carbohydrate. They had quite a number of patients on diets containing from 187 to 354 grammes of carbohydrate; with these large amounts of carbohydrate the fat given ranged between 70 and 90 grammes, and almost never above 100 grammes. With carbohydrate and fat, the more the one went up, the more the other must come down.

All the patients on these very high carbohydrate diets were progressing satisfactorily; the average amount of insulin per day was about 36 units. However, in spite of these experiences, they felt that it was wiser to adopt a middle course, giving, as stated above, about 150 grammes of carbohydrate.

The most important factor in the diabetic diet was the total calories. This determined the burden of the pancreatic function and the insulin requirements. While the diet should be sufficient to maintain strength, weight and full capacity to perform the normal occupation in life to which the patient was habituated, it should not promote over-nutrition. Provided over-nutrition was avoided by careful regulation of the total calories, the proportions of carbohydrate, protein and fat might be varied considerably without greatly changing the insulin requirements.

Progressive Muscular Atrophy.

Dr. MAUDSLEY showed a male patient, aged twenty-one years, who had been attending the diabetic clinic since 1927. His urine was sugar-free with insulin and dietetic treatment. Three months before it was first noticed that there was some wasting of the first interosseous muscle, together with some wasting of the thenar eminence of his left hand. Dr. Maudsley said that there had never been any subjective or objective sensory phenomena; no fibrillary muscular twitching had been observed.

On examination there was wasting of the first, second and third dorsal interossei muscles and flattening of both thenar and hypothenar eminences. The upper limb reflexes on the affected side were slightly increased. There were no other neurological signs.

X ray examination of the cervical region showed that there was an abnormally long transverse process to the seventh cervical vertebra.

It was considered possible that pressure on the brachial plexus was giving rise to the paralysis of the hand. This seemed scarcely likely in the absence of any sensory changes. A diabetic peripheral neuritis could be ruled out for the same reason.

The case appeared to be one of progressive muscular atrophy, notwithstanding the absence of fibrillary tremor.

Ulnar Nerve Lesion.

Dr. Maudsley's next patient was a man, aged sixty-three years. Five years before he commenced to have weakness of the fourth and fifth fingers of his right hand. This progressed to a complete ulnar nerve lesion with typical semi-flexion contracture of the fourth and fifth digits and wasting of the *flexor profundus digitorum* muscle. There was loss of all forms of sensation over the skin area supplied by the ulnar nerve. A month before slight contraction of the little finger of the left hand was first noticed. There was loss of sensation to pin-prick and light touch over the ulnar surface of the hand and little finger, showing evidence of an ulnar nerve lesion on the left side. The patient was edentulous, and no focus of infection could be found. The Wassermann test yielded no reaction. There were no other neurological signs.

Dr. Maudsley said that the possibility of an early syringomyelia came under discussion, but in view of the absence of other motor or sensory phenomena this diagnosis could scarcely be entertained. The aetiology of the ulnar nerve lesions in the right side and the commencing similar lesion in the left side was obscure.

Disseminated Sclerosis.

Dr. Maudsley also showed a man, aged twenty-one years. Two years ago he gave a history of dragging the right foot after he had walked any distance. At the same time he noticed some paræsthesia in his right hand; he often could not recognize objects placed in his right hand, and would drop things without realizing that he had done so. At that time no objective neurological signs were noted. His right leg improved, but some paræsthesia of his hand remained.

On examination the optic disks were normal in appearance. There were no cranial nerve defects. The deep reflexes were somewhat exaggerated, those on the right side of the body slightly more than those on the left. There were no objective sensory changes. The plantar reflexes were flexor in type. The abdominal reflexes in the upper and lower quadrants on both sides were absent.

Dr. Maudsley said that the absence of the superficial abdominal reflexes in this case was a most significant feature. This sign, together with the history of paresis with remission would suggest strongly the probability of disseminated sclerosis.

(To be continued.)

NOMINATIONS AND ELECTIONS.

THE undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

Bayldon, Francis Wood, M.B., B.S., 1930 (Univ. Sydney), Taree.

McCormack, Patrick Edward, M.B., B.S., 1930 (Univ. Sydney), Queanbeyan.

Obituary.

CHARLES ALBERT MÜLLER.

WE regret to announce the death of Dr. Charles Albert Müller, which occurred at Sydney on September 22, 1932. Two of his colleagues who wish to remain anonymous, write as follows:

In these days of pushful forwardness it is a sort of obligation of duty and personal esteem to speak in the pages of our journal of one who certainly spent his life in useful work and never courted the limelight. Of such was Charles Müller. Born in Brisbane over sixty years ago, he was a very successful pupil at the Brisbane Grammar School and later studied medicine at Melbourne, where he again showed himself an able and diligent student. After graduation he came to Sydney as a resident medical officer in Saint Vincent's Hospital. There he gained at once the trust and liking of all the honorary medical staff. Their trust because of his keenness, capacity and common sense; their liking because of his kindly ways, unfailing industry and honest character. After due service as a resident he went into practice in Sydney and was put upon the honorary surgical staff of the hospital. He proved himself a sound all-round surgeon, and in gynaecological work had special opportunities and aptitude. From his huge practice, indeed, he could always fill his beds with his own patients, mostly, alas, needing abdominal section.

He led, I fear, a hurried, harassed life, having always more to do than was in his own best interests. He took a holiday hardly ever, and probably his work sometimes suffered in the rush of the day's overwhelming calls. He never had time or inclination, I think, to attend professional meetings, which was wrong. I doubt if he ever read or wrote a paper. Thus his wide practical experience and sound clinical knowledge had no outward expression and has died with him; and the pity is that this should have been so.

In later years his health failed, his activities were curtailed, and he retired still more into himself and a

narrowed sphere of work. I doubt if the general body of the profession ever realized what an able practitioner he was, and especially what an honest, unselfish, unmercenary soul worked unobtrusively among his fellows. Happily, some of his old colleagues always recognized his merits and knew what a fine fellow this man was whom they called friend. If, indeed, also they regretted his tearing daily life of labour and his inability to do less practical and more academic work, they at least appreciated his fine qualities and shrewd sense. There must be thousands of patients who miss him, and among the small circle of his professional intimates his loss is a real sorrow.

AN OLD COLLEAGUE.

I remember C.A.M. above all for his great sense of humour, his round red face bursting with merriment and his twinkling eyes. He was the most charitable of men, and was ever ready to do or give without thought of return. Indeed, he was a most capable surgeon, but alas, smothered beneath the trivialities of a busy practice. His patients loved him. He hid his kindness with sometimes rough, cheery words, for he was at bottom a very shy man. In later years he crept into a corner and shunned the old associations, but he leaves a memory of one who lived laboriously and who left many of us greatly beholden to him.

ANOTHER OLD COLLEAGUE.

ARCHIBALD WARDEN GRAVES MURRAY

WE regret to announce the death of Dr. Archibald Warden Graves Murray, which occurred on September 23, 1932, at Colac, Victoria.

Correspondence.

HOSPITAL PRACTICE IN NEW SOUTH WALES.

SIR: The article in the journal of August 20 (pages 249 to 251) on hospital practice in New South Wales, by Dr. R. B. Wade, is certainly useful, for it is very evident that many practitioners know nothing of the *Public Hospitals Act, 1929*, though it has been three years in force. There are some points in the article which require examination.

On page 251, in the discussion of forms of admission, it is stated:

The clause in Forms 4 and 5, "and I agree that the hospital charges shall have priority to any professional charges due to me for the treatment of the patient, and that I will, before taking any proceedings for the recovery of my charges, give twenty-one days' notice of my intention to the hospital", and regulation 31, give the medical practitioner the right to recover legally his fees, if unpaid.

This clause would appear to give the hospital the right to collect as well as recover, subject to the twenty-one days' notice by the medical practitioner of intention to take proceedings, all fees payable before the medical practitioner may do so. The Hospitals Commission, however, interprets this to mean that the medical practitioner is at liberty to make his own arrangements as to fees and to collect them when he likes, except when both hospital and medical practitioner's fees are unpaid, the hospital has priority of claim to take proceedings; in other words, medical practitioners cannot take proceedings to recover their fees unless they have given the hospital twenty-one days' notice of their intention to do so.

The interpretation, said to have been placed by the Hospitals Commission on the clause quoted in Forms 4 and 5, would appear to be an outstanding example of an attempt to interpret black as being white or at most no darker than a pale grey. The words of the clause would

appear to be quite definite, giving the hospital priority in its charges to any professional charges, not only those incurred in the hospital, but also to any already due when the form is signed on the admission of the patient. Apart altogether from any question of the *Public Hospitals Act*, any sensible man who signed an agreement in that form would be bound, in my opinion, to take it in the sense which I have given. There is a further point to be considered in this matter of interpretation, and that is that it is not the function of the Hospitals Commission to interpret the meaning at all. Interpretation is the function of the courts, and I would not care to have to depend on the opinion of the Hospitals Commission if the question came to law. Lord Hewart had something to say some time ago regarding bureaucratic government and interpretation of the law by irresponsible public servants. In this case the usual process seems to have been somewhat reversed, as apparently an attempt has been made to twist plain English into a meaning it will not bear, in favour of the medical practitioner.

Another aspect of the question which deserves consideration, is whether the hospital has any moral right at all to priority over the medical practitioner in the matter of recovery of fees. At the annual meeting of delegates of Local Associations with the New South Wales Branch Council on October 2, 1931, the following resolution was carried.

That the Council of the New South Wales Branch endeavour to have the Regulations under the *Public Hospitals Act, 1929*, amended by the deletion therefrom of Regulation 31 and the alterations of Forms 4 and 5 under the Regulations, in order to place the practitioner on an equal footing with the hospital in the matter of recovery of fees due by patients.

In my opinion the Council and the Hospitals Committee would be far more advantageously occupied in attending to this matter than in placing any reliance on the "interpretation" of the Hospitals Commission.

In regard to Regulation 32 (page 251), the statement that "no recommendation has been made by the suggested association or body" calls for notice. In the annual report of Council, 1930-1931 (*THE MEDICAL JOURNAL OF AUSTRALIA*, April 4, 1931, page 422) is the following paragraph:

Public Hospitals Act, 1929. A letter was received from the Hospitals Commission requesting that the Council would consider a proposal that the scale of fees chargeable by medical practitioners for attending intermediate patients in public hospitals should not exceed fifty per centum (50%) of the recognized scale of fees chargeable to full private patients. After communicating with the Local Associations of Members, it was decided to recommend to the Hospitals Commission that the fees chargeable by medical practitioners for attending intermediate patients in public hospitals should not exceed fifty per centum of the fees usually charged to private patients in the district in which the hospital is situated.

In passing it must not be thought that the Local Associations were all in favour of this proposal. Several were violently opposed to it. At the annual meeting of delegates above mentioned, the following resolution was carried:

That it be the policy of the New South Wales Branch that the matter of fees for treatment of intermediate patients in public hospitals be settled by arrangement between the patient and the attending practitioner.

It will be seen from Dr. Wade's article that the imposition of an upper limit of 50% of the usual fee does not produce equitable results. In the case of large metropolitan hospitals, if the usual fee of the practitioner attending the hospital is, say, £100 for a major operation, his upper limit for intermediate patients is £50. In other places the upper limit for the same operation might be as low as £10. This in spite of the fact that the patient might quite well be able and willing to pay £15 or £20 or more for the operation. The proper solution of the matter, of course, is that in the case of either the inter-

mediate or private part of a hospital, the medical practitioner should be able to make his own arrangements with the individual patient regarding fees, apart altogether from the portion of the hospital the patient wished to enter.

Yours, etc.,

J. R. RYAN.

Lismore,
New South Wales,
August 22, 1932.

Books Received.

COLONIC IRRIGATION, by W. Kerr Russell, M.D., B.S.; 1932. Edinburgh: E. and S. Livingstone. Demy 8vo., pp. 199, with illustrations.

THE PHYSICAL MECHANISM OF THE HUMAN MIND, by A. C. Douglas, M.B., Ch.B.; 1932. Edinburgh: E. and S. Livingstone. Demy 8vo., pp. 265, with illustrations. Price: 15s. 6d. net.

RECENT ADVANCES IN ANÆSTHESIA AND ANALGESIA, by C. L. Hewer, M.B., B.S.; 1932. London: J. and A. Churchill. Demy 8vo., pp. 195, with 64 illustrations. Price: 12s. 6d. net.

Diary for the Month.

- Oct. 10.—New South Wales Branch, B.M.A.: Organization and Science Committee.
Oct. 11.—New South Wales Branch, B.M.A.: Ethics Committee.
Oct. 13.—New South Wales Branch, B.M.A.: Clinical Meeting.
Oct. 14.—Queensland Branch, B.M.A.: Council Meeting.
Oct. 18.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Oct. 19.—Western Australian Branch, B.M.A.: Branch.
Oct. 25.—New South Wales Branch, B.M.A.: Medical Politics Committee.
Oct. 26.—Victorian Branch, B.M.A.: Council.
Oct. 27.—South Australian Branch, B.M.A.: Branch.
Oct. 27.—New South Wales Branch, B.M.A.: Branch.
Oct. 28.—Queensland Branch, B.M.A.: Council.

Medical Appointments.

Dr. S. H. Davison has been appointed Government Medical Officer at Blayney. New South Wales.

Dr. K. E. Moore (B.M.A.) has been appointed Government Medical Officer under the provisions of Section 3 of *The Miners' Phthisis Act, 1922*, Western Australia.

The undermentioned appointments have been made in the Adelaide Hospital, South Australia: Honorary Clinical Assistant to Medical Section, Dr. R. G. Burnard (B.M.A.), Dr. E. F. Gartrell (B.M.A.), Dr. H. W. Wunderly (B.M.A.); Honorary Clinical Assistant to Surgical Section, Dr. G. H. Burnell (B.M.A.), Dr. W. J. W. Close (B.M.A.), Dr. A. F. Hobbs (B.M.A.); Honorary Clinical Assistant to Ophthalmic Section, Dr. M. Schneider (B.M.A.); Honorary Clinical Assistant to Skin Section, Dr. W. C. T. Upton (B.M.A.); Honorary Anæsthetist, Dr. H. E. Pellew (B.M.A.).

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser", pages xii and xiii.

HOBART PUBLIC HOSPITAL, HOBART, TASMANIA: Junior Resident Medical Officer.

LAUNCESTON PUBLIC HOSPITAL, LAUNCESTON, TASMANIA: Resident Medical Officer (male).

SYDNEY HOSPITAL, SYDNEY, NEW SOUTH WALES: Honorary Assistant Urological Surgeon, Honorary Assistant Dermatologists.

THE UNIVERSITY OF SYDNEY, NEW SOUTH WALES: Dental Research Scholarship.

VICTORIAN EYE AND EAR HOSPITAL, MELBOURNE, VICTORIA: Resident Surgeons.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmalm United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phoenix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane Associated Friendly Societies' Medical Institute. Mount Isa Mines. Toowoomba Associated Friendly Societies' Medical Institute. Chillagoe Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 297, North Terrace, Adelaide.	All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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